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FRACTURE OF THE NECK OF THE FEMUR

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Fracture of the neck of the femur has the highest death rate of any simple fracture of the long bones in advanced middle age or old age. Crippling and permanent disability from nonunion and stiff joints have afflicted nearly half those who survive. The high mortality and serious disability have led to trial of operative internal fixation for many years, with increasing frequency during the past few years.

RELATIVE RESULTS OF CONSERVATIVE AND OPERATIVE TREATMENT

Expert opinion was sought as to the relative value of conservative and of operative treatment by consulting textbooks devoted entirely to fractures and the sections devoted to fractures in systems of surgery.[1] There is uniform pessimism concerning prognosis and results, especially with patients over 60 years of age or afflicted with medical complications. All authorities report infrequent bony union and considerable disability. The greater number recommend Whitman's abduction method as the treatment of choice. No comprehensive statistics are given. Speed classes this fracture as the "unsolved fracture."

Recent surgical literature gives a somewhat different picture: 2,074 cases were collected from various sources.[2] Of the patients, 1,094 were conservatively treated, most of them by the Whitman method, with an average of 51 per cent of bony union. This figure practically agrees with that of Böhler of Vienna, a widely recognized authority on fractures.

There were 980 patients treated operatively, and all methods were used: bone pegging, open operation with the Smith-Petersen nail, blind nailing with the Smith-Petersen nail, multiple nailing, and screw and bolt fixation. The average percentage of bony union was 78. Obviously, 27 per cent shows a substantial gain in bony union in favor of internal fixation, but this is far less than that shown by the percentages of a few experts: Moore 96, Johansson 93, Mathieu 92, Watson-Jones 91 and Böhler 88. Bone pegs have poorer results than stainless steel or ordinary steel devices. This study seems to give a fair cross section of the results which might be expected, for some surgeons report as few as two cases of treatment by their special method. When the skill is acquired which many surgeons have with conservative methods, poor results should be mainly from aseptic necrosis of the head and preexisting medical complications.

Read before the Section on Surgery, General and Abdominal, at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

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Mortality is the question of first importance. Conservative methods give an average rate, taken from several sources, of approximately 25 per cent, while the average taken from 980 recent cases is only 9 per cent for blind nailing, a gain of 16 per cent. When it is remembered that cases for Whitman's abduction must

Fig. 1.—The templet disassembled, with the nail which is used in the tail and three Moore pins.

be carefully selected, with bad risks excluded, this figure becomes more significant, for no such careful selection is made by many advocates of internal fixation.

FRACTURE OF THE NECK OF THE FEMUR IN SMALLER COMMUNITIES

Textbooks on fractures and the more important articles dealing with these injuries have all been based on the experience of fracture clinics in large cities and of orthopedic surgeons, specialists in bone and joint disease. At least one third of all fractures, however, must be treated by rural practitioners and small town surgeons, for transportation to the larger centers is impossible in many cases because of the serious general condition and the financial circumstances of the patient.

We have attempted to get an estimate from rural communities and the smaller cities by sending questionnaires to physicians within a radius of 100 miles from

Results of Treatment by Rural Practitioners and Surgeons in Small Cities

Form of Treatment	Good Results Without Use of Crutch or Cane, Per-centage	Fair Function With Crutch or Cane, Per-centage	Poor Function; Patient About on Crutches, Per-centage	Patient Living; Unable to Be About, Per-centage	Patient Died, Per-centage
Fracture ignored....	15.0	22.5	2.5	2.5	57.5
Sand bag.....	29.4	29.4	13.1	4.9	28.1
Buck's extension....	56.8	23.8	3.9	2.7	12.8
Whitman's abduction.....	48.0	20.0	4.0	12.0	16.0
Anderson's splint....	71.4	19.1	....	....	9.5
Smith-Petersen nail.	28.5	14.2	14.2	....	42.8

Ithaca. These physicians are general practitioners and small town surgeons, whom we know personally, who have sent patients to us for various surgical operations; in more than one third of the instances either the physician or members of his family have been our patients. They are of better than average professional ability, as a group conscientious, and of wide general experience. The small town surgeons include some of exceptional education, training and experience; most of them lack the special experience of surgeons in large clinics and of orthopedists.

Reports of 573 cases have been received. All the physicians gave valuable information. Full data concerning results were given by 295. The forms of treatment and the percentage of good results in relation to the number of patients treated by each method (not the total treated by all methods) are given in the accompanying table.

It will be noted that more than a third of the patients were treated by ignoring the fracture or using the sand bag because of their bad condition. These obviously makeshift methods of treatment cannot be expected to give satisfactory results. The death rate for these two methods (85.6) is very high, 57.5 per cent for disregard of the fracture and 28.1 per cent for treatment by sand bags. Even with these makeshift methods several recoveries with fair results are noted; there were 15 per cent of good results when the fracture was entirely ignored and 29.4 per cent when only sand bags were used. Several of the patients were over 80 years of age and in poor general health.

Buck's extension was the most commonly used procedure, nearly one third of the patients being treated by this method. Good results, walking without crutch or cane, were reported in 56 per cent of the cases, this percentage being approximately 9 per cent higher than that for the Whitman method in this series and also better than that usually reported. The death rate was approximately the same as that reported from large clinics, in spite of lack of facilities and nursing care in many cases. That the results of conservative methods are better than most reported from larger centers may be due in part to the sturdy character of the patients, most of whom were accustomed to hard work and plain living. Also it is fair to state that general practitioners of rural communities and the smaller cities generally give personal and faithful care to patients, in many instances better than that of an inexperienced intern.

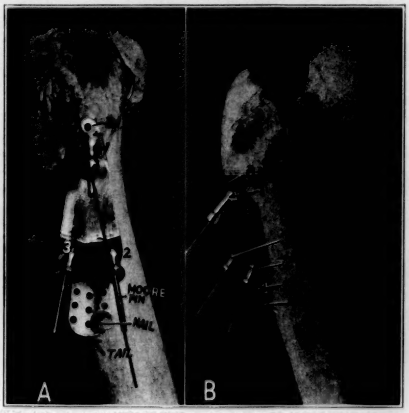

Fig. 2.—The templet in position in the right femur, with Moore pins, or nails, already inserted through guide tubes. The straight line down the center of the outer side of the femur, in *A*, shows how guide tubes 1 and 2 must be alined for a bone on the right side. *B*, a lateral view of the templet in place, shows the apex of the templet (*a*) hooking over or cupping the line of the vastus externus.

The results did not approach the average for internal fixation by experienced operators. Most small town surgeons are conscientious enough not to undertake a surgical procedure of major importance when they feel that they lack experience or facilities, which doubtless accounts for the small number of operations. The need for roentgenograms in both the anteroposterior and the

lateral position cannot be met by most rural practitioners. Internal fixation was used in two cases with excellent results by a man of surgical experience and ability. It seems evident that most of the unfortunate results were due to lack of study of methods and lack of general surgical experience on the part of those who

Fig. 3.—Right femur. *A*, first stage in removal of templet; nail in tail pulled out and guide tubes unscrewed. *B*, templet coming off leaving pins in place.

used them. We believe that if the men of the smaller cities would cooperate and refer their work to a few who, through study, an effort to acquire experience and natural aptitude, are fitted for special work, it would be possible to reduce the death rate decidedly and to save a great deal of unnecessary suffering and expense.

We report on five patients treated by internal fixation, all of whom survived operation. Only one of the five could have been considered a good risk for a major surgical procedure. The others were all of advanced age, with general conditions which contraindicated such a procedure.

REPORT OF CASES

CASE 1.—A woman aged 69, admitted Jan. 26, 1938, the day of fracture, was discharged April 9, after ten weeks and three days of hospitalization. A roentgenogram taken January 27 showed an intertrochanteric fracture, with a split off of the lesser trochanter. Nailing was performed February 10. There were marked senility and decrepitude, with kyphosis of the spine. The patient sat up in a chair two days after operation and walked on crutches seventeen days after operation. She had had a temperature of from 101 to 103.2 F. continuously before the nailing. She could walk without crutch or cane four months after operation.

CASE 2.—A woman aged 75, admitted March 11, 1938, two weeks after fracture, was discharged April 14, after four weeks and two days of hospitalization. A roentgenogram taken March 11 showed a medial fracture of the neck of the femur on the right side. March 14 nailing was performed. March 17, the third day after operation, the patient sat in a chair, and March 20, the sixth day, she walked on crutches. She had high blood pressure, dyspnea, arteriosclerosis and obesity. She was very happy at the relief of pain. She was still on crutches three months after operation.

CASE 3.—A man aged 72, admitted Feb. 28, 1938, the day of fracture, had nailing performed March 4. He sat up in a chair March 7, the third day, and walked on crutches March 14, the tenth day. There were myocardial degeneration, diabetes and arteriosclerosis. The patient was still in the hospital, with boils and urticaria, and still on crutches three months after operation.

CASE 4.—A woman aged 57, admitted Sept. 18, 1937, the day of fracture, and discharged November 18, was operated on September 23. The fracture was a simple, complete, transverse fracture of the neck of the right femur near the head. The first roentgenogram was taken September 18. A roentgenogram first suggested bony union November 7. The patient sat up in bed September 26, the seventh day after operation, and in a wheel chair October 5. She went back to bed on the advice of the roentgenologist, and she sat up again November 11. She walked on crutches November 15. There was no complicating physical or mental ailment. She walked without a cane or crutches in six months.

CASE 5.—A woman aged 65, injured Oct. 11, 1937, was admitted October 12. The first roentgenogram was taken the day of admission, and the first operation, nailing, was performed October 13. The nails were shortened October 15. An operation performed October 25 was necessitated by failure of the roentgenologist to take a lateral view. There was no serious physical handicap except marked obesity. The cooperation was poor. March 30 it was seen that absorption of bone around the nails with shortening and atrophy due to disuse had permitted the nails to penetrate into the acetabulum. The roentgenologist was doubtful as to whether union had occurred, but weight bearing was advised. The patient sat up in a wheel chair October 20 and walked on crutches November 23. She died nine months after operation of agranulocytosis or agranulocytic angina in association with infection of the mouth.

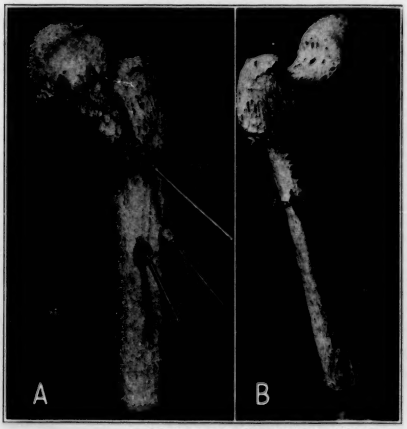

Fig. 4.—Left femur. *A*, nuts screwed and wire applied to steady pins and prevent nuts from running off backward. *B*, excess of pins cut off.

It seems evident that four of the five patients were of the class who generally, because of their serious condition, are treated by ignoring the fracture or at most are treated by sand bags and rest in bed.

A GUIDE (TEMPLET) FOR DIRECTING NAILS

The desirability of some appliance for directing nails, screws or other supporting devices so that they may be properly placed has been recognized by many surgeons. At least seven devices have been described, most of

which are too complicated and would be too expensive for the average surgeon of small city hospitals.

Recognizing the importance of a simple appliance by means of which nails could be placed accurately, one of us (M. B. T. Jr.) devised a nail director, or templet. The one depicted is so constructed that it will guide three nails, as suggested by Austin Moore, by means of

Fig. 5.—Right and left femur, same patient, demonstrating the marked structural difference between the two and showing that the appliance is adaptable to either side and that due allowance has been made in figuring the angles of the guide tubes or templet to provide for the variation. Roentgenograms of these bones (figs. 6 and 7) prove that the pins are in a satisfactory position.

three tubes which can be removed after the nails are in position. A study of the femur by Gaenslen (*Journal of Bone and Joint Surgery*) shows that the cross section of the neck, the target to be aimed at, is roughly 1.8 by 2.5 cm. in diameter. It has been found by experiment with a large number of femurs that individual differences are not great; the templet has been successful in all cases in which it has been tried experimentally. Furthermore, it can be adjusted for use on the right or left side. A modification for use with a single Smith-Petersen nail or two small-flanged nails, as satisfactorily employed by Louis A. Goldstein of Strong Memorial Hospital, University of Rochester, we believe could be readily made. Patent has been applied for by the maker of the templet, Lawrence Scott of Ithaca, N. Y.

It is understood that the fracture must first be properly reduced. In using the templet, right or left femur, the upper curved end hooks over the vastus line. Guide tube 1 should be placed exactly over the middle of the femur. The upper opening of tube 1 is about one-fourth inch below the vastus line.[3]

For the right femur one places the drill through the guide tube and drills through the compact bone with the drill parallel to the surface of the operating table (figs. 2 and 3). The templet must be so adjusted that the line between the drill hole already made and tube 2 will be parallel to the table and in the center line of the femur. A drill hole is then made through one of the smaller holes in the "tail" of the templet, and a small ordinary nail or some similar object is placed in this hole to hold the templet in position and prevent side slip. A drill hole is made through the compact tissue of the femur through tube 2, and nails ("nail" is used by Moore instead of "pin" as shown in the illustration) are entered in tubes 1 and 2 to hold them in place. A third hole is then drilled, through tube 3, and the nail is placed.

If the left femur is to be operated on, tubes 1 and 3 are placed parallel to the edge of the table and on the center line of the femur, the nail for tube 2 being placed last (fig. 4). When the nails have been inserted the templet can be removed by unscrewing the guide tubes and removing the nail in the tail section. Nails should be inserted at a distance approximately three-fourths inch less than the length of the neck as shown by a roentgenogram taken in the anteroposterior position after reduction. This is because the x-ray image is a projected one, larger than the bone itself, as stated by Moore. Resistance of the bony cortex indicates that the head has been reached.

Roentgenograms should now be taken in the anteroposterior and lateral positions to determine the angle and depth of the nails. If these are correct, nuts should be screwed on and the nails cut off to approximately one-eight inch. The fracture can be impacted by one or two fairly sharp blows on the nails. A wire about the nails (fig. 4) holds them and keeps them from spreading or withdrawing.

EXPERIMENTAL STUDY OF METHODS OF INTERNAL FIXATION

Determination of the relative value of the flanged nail (the Smith-Petersen nail, its modifications and other similar nails), of multiple nailing and of the use of screws was attempted by testing experimentally fractured fresh bones fixed by these methods. Resistance to force in the weight-bearing position and torsion were estimated in testing machines of the Department of

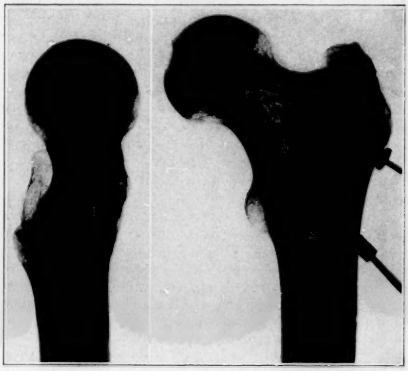

Fig. 6.—Right femur; pins in a satisfactory position.

Experimental Engineering of Cornell University. A large amount of anatomic material furnished through Drs. A. T. Kerr and J. W. Papez of the Department of Anatomy, Cornell University, made this work possible. Tests of the strength of various methods of internal fixation were under the direction of Prof. Will Sawdon of the Department of Experimental Engineering. The

3. Operative experience, after this paper was written, shows that nail number one would best be first placed and control of position made by x-ray examination. Then the templet is slipped over the nail and it will satisfactorily guide the other two nails.

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placing of nails, screws, bolts and other appliances for internal fixation must be accurate, and results must be checked by roentgenograms in two planes. The neck of the femur was sawed through in an effort to determine how much the nails alone would hold; it is evident that when the bone is broken there are jagged points which when impacted act somewhat like the matching or dovetailing of wood. The Moore nails alone, with a sawed-smooth surface, will carry a load of 100 pounds or more in some instances. Bones broken, nailed and

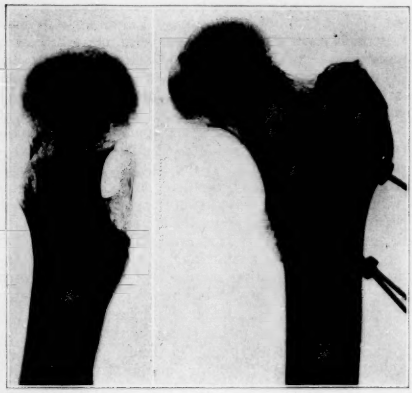

Fig. 7.—Left femur; pins in a satisfactory position.

impacted have carried much greater loads, up to 300 pounds. Smith-Petersen nailing carried about the same load as the least efficient Moore nailing.

The conclusions to be drawn from the experimental work, as summarized by Professor Sawdon, were as follows: 1. Repair of actual fracture with proper reduction gives much greater support than does repair with sawed or smooth surfaces. 2. Support rendered by cancellous bone is much greater than would be expected. 3. There is a distinct spring, or elastic property, to the Moore nails which tends to restore the fracture to the original position after compression. 4. There is a considerable load capacity to the Moore nails after apparent yielding of the fracture. 5. There is little elastic property in the Smith-Petersen nail, and consequently there is crushing or destruction of the cancellous bone and distinctly less recovery. 6. The exact position of the Moore nail is not of fundamental importance in determining its holding capacity. 7. The Moore nail has better contact-holding properties than the Smith-Petersen nail or, in other words, is better able to hold fractured fragments together, since the Smith-Petersen nail is easily withdrawn after the test. Pliers were required to extract the Moore nails in every case, even after vigorous testing, while the Smith-Petersen nail could be withdrawn easily with the thumb and forefinger.

In essence these conclusions signify that the Smith-Petersen nail does not hold the fractured surfaces in apposition as well as the Moore nail and hence does not provide the opportunity for union.

Important considerations related to recovery are (1) immediate relief from pain and surgical shock, (2) immediate freedom from confinement in fixation apparatus and bed, which so frequently has led to fatal hypostatic pneumonia, (3) raising of the patient's morale, the relief from pain and the ability to move about freely greatly influencing the will to live as well as to recover function. These conditions have been met successfully by internal fixation in many cases by a number of surgeons.

ABSTRACT OF DISCUSSION

DR. KELLOGG SPEED, Chicago: The scope of this paper, including as it does morbidity, mortality, choice of treatment and personal experience with internal fixation of fracture of the neck of the femur, makes it difficult to discuss. There seems no doubt that internal fixation has come to stay, that it will be practiced everywhere and that it is a godsend to many, in offering early freedom from pain and mental refuge in the faith in mechanical contrivance or fixation hopefully accepted by the patient, and often by the doctor, as a way out of an immediate difficulty. Ways and means of fixation are probably of secondary importance compared to these two factors, namely immediate relief of pain and restoration of confidence and mobility of varying degree for the patient. The choice of fixation lies with each physician who uses that type which may be employed best with the least disturbance of or trouble to the patient. Each agent, flanged nail, metal pin, bone transplant, screw or other device, may be open to certain objections, but at given distances throughout the country one should be able to find surgeons satisfactorily trained to use with reasonable safety one device or the other to alleviate human suffering in the presence of this frequently fatal fracture. Devices for directing the nail or pin are not fool proof; they have been in existence more than fifty years and are not yet universally adopted. The one essential, regardless of the agent of fixation or its method of introduction, is reduction of the fracture, controlled by the x-rays. The insertion of the internal agent must be done in conformity with strict aseptic principles, and the final result as to bony union, viable head and freedom from secondary changes, such as aseptic necrosis, flattening, loss of cartilage and ultimate painful coxitis, must lie in observation of the patient over a long period and a prolonged study of the condition and of retrieved specimens obtained after treatment. Internal fixation followed by early weight bearing seems to act at cross purposes. Some of the advocates of the method are now recanting their remarks on early weight bearing and restraining the patients for from sixteen to twenty-four weeks before allowing freedom in walking. A patient walking on crutches may be a long way from complete cure when bony union or the health of his bone is concerned, but at least he is alive and active. Study of clinical results, coupled with progressing pathologic study, will eventually give practitioners better control of this fracture.

DR. E. W. CLEARY, San Francisco: The authors are to be complimented on the courage and determination with which they have pursued this investigation and on the ingenious device used for directing the Moore nails. Dr. Austin Moore himself feels that no such device is necessary for directing the nails—that he can guide their introduction as he puts them in by feeling with the hand chuck that he uses. I have verified this observation. I agree with the authors that internal fixation is the great problem in dealing with this fracture today. The procedure falls into four different steps. I agree with Dr. Speed that the first step is reduction. After reduction there must be some means of accurately localizing the position of the fractured bone as well as determining the extent of the reduction, and then there must be some means by which the surgeon can bring the information afforded by the localizing x-rays into his operating field in order that he may so place his fixation device as to be sure of its effectiveness. Some years ago I started to work on a device which would first of all hold the reduced fracture in a preferred position for x-ray localization and for the surgeon's subsequent fixation. The advantages of the flexed thigh position had already been emphasized. I found no adequate device for holding the leg in this position, and with a great deal of trial and hard work I have developed an accessory table which is an effective aid in the three last of

the four steps in dealing with this fracture. It fixes the patient and holds the reduced fracture firmly in position for the operation. It provides for standardized x-ray localization in two planes, and it provides by means of exact mechanical instruments, which may be sterilized, for the transfer of the exact x-ray localization into the aseptic field of operation, where it is utilized by the surgeon in directing the nail or fixation device of whatever character he may choose.

DR. WALTER G. STERN, Cleveland: Fifteen years ago Dr. Phil Kreuscher and I advocated the then rather new method advanced by Dr. Royal Whitman of New York, which consists in complete reduction of the deformity caused by the fracture by means of extension, internal rotation and abduction of the femur and fixation of the limb in this position until either union has taken place or nonunion has been found inevitable. These principles are as sound today as they were then, so that today only the method of fixation is being debated. To some of the members this "immolation in plaster" is a terrible thing. They never apply the casts themselves and do not have the mechanical apparatus to care for cases in which casts are required, or the family does not care to put a hook in the ceiling to lift the bed so that the patient can be standing up part of the time. Therefore they have gone back to something easier and more comfortable, internal fixation by means of metal devices. J. B. Murphy forty-five years ago advocated the use of the then new round wire nail, and I have roentgenograms of the second patient in whom he used a nail forty-four years ago. Nonunion was the result, and the man walked on that nonunited limb for twenty years and worked as a roller in a rolling mill until the nail got so badly bent that I had to take it out. Jones of Grass Valley, Calif., and Roger Anderson of Seattle have also worked on this problem of fixation by means of the "well leg traction" methods, and for a while some surgeons thought that this might be the solution; but the thing gets away from one, the reduced bones are not kept in position to heal and the method had to be abandoned. M. N. Smith-Petersen revived the old and discarded method of nailing the fragments together, with an ingenious three-flanged nail, the chief advantage of which lies in the fact that when it is well placed in a solid head it really prevents the rotation of the fragments on each other. I am going to issue a word of warning: Even under local anesthesia with old persons the introduction of pins or nails is a major operation. One of the major medical societies will soon come out with the results of a questionnaire on this subject in which it will be seen that the death rate from internal fixation in these cases is 9 per cent plus. A method which is rapidly becoming popular in Europe is the high Schanz osteotomy, sometimes called the Lorenz bifurcation or Watson-Jones subtrochanteric osteotomy.

DR. MARTIN B. TINKER, Ithaca, N. Y.: I am much gratified by the active discussion which our paper has provoked. The careful preparation of all the discussions has added much to the value of the presentation. No surgical method is perfect: all have their weak points. With regard to the remarks of Dr. Stern, it seems to me that one is reverting when one contemplates subtrochanteric osteotomy. He mentioned the danger of shock even with local anesthesia, on account of the time required. What does one get into with subtrochanteric osteotomy? That is a major procedure to begin with, whereas in the hands of surgeons who properly qualify themselves this other operation need not last a long time and need not be associated with much shock. Moore operated in thirty-five minutes and has had no operative deaths in sixty-nine cases in which he has used his pins. Sven Johannsen of Sweden, who has reported more than a hundred cases in which he himself has used the Smith-Petersen nail, had a mortality of 9 per cent. It seems therefore that when all is said and done it is a question of the surgeon's preparation properly to perform this technic, whether it is with the Smith-Petersen nail or three nails or two screws or whatever agent of internal fixation appeals to one. It is necessary to work hard, do a lot of study and exercise great care if one is going to do work of this kind and have success. The work that my associates and I have presented is perhaps not the final solution, but certainly internal fixation is the best method available at the present time.

INTRAVENOUS ALIMENTATION

WITH SPECIAL REFERENCE TO PROTEIN (AMINO ACID) METABOLISM

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ST. LOUIS

Intravenous (as a method of parenteral) alimentation becomes important whenever the nutritional needs of the body cannot be met by oral feeding; it becomes essential when death threatens because of nutritional deficiencies which can be remedied in no other way. These nutritional needs comprise six elements: water, salts, carbohydrate, protein, fat and vitamins. As far as water, salts and carbohydrate are concerned, intravenous alimentation is now a commonplace and extensively used procedure. For example, at the Barnes Hospital 125 liters and at the St. Louis City Hospital 200 liters of saline and dextrose solutions for subcutaneous and intravenous administration are used daily. Why have the remaining three nutritional elements been overlooked? If carbohydrate is important, why not protein, fat and vitamins? The answer lies partly in lack of information on the real needs for protein, fat and vitamins in patients more or less completely, though temporarily, unable to ingest any food by mouth. Another probable reason is the chemical complexity of these nutritional elements, which makes it difficult to prepare them for parenteral use. Fat, it is true, has been prepared in a fine emulsion for intravenous injection.[1] It is questionable, though, whether fat is really essential for maintenance, at least for short periods. Even for growth, fat has been shown to be dispensable, at least if one unsaturated fatty acid, linoleic acid, is provided.[2] It would seem that the other lipids can be manufactured from carbohydrate and protein. Vitamins, to be sure, are rapidly being isolated in pure form and several (B_1, B_2 C and nicotinic acid) can now be given intravenously. How important are they, however, for relatively short periods of nutritional deficiency? Since many of the vitamins are stored in the liver and elsewhere, these accessory food factors may perhaps be disregarded, unless of course prolonged parenteral alimentation becomes necessary. It must be admitted nevertheless, that with certain sick patients the need for one or more vitamins may be an important part of their nutritional needs. We shall be more concerned in this paper with the need for protein; it should be emphasized, however, that it is difficult if not impossible to consider one element independently, since each is closely related to the others in its metabolic behavior.

INDICATIONS FOR INTRAVENOUS ALIMENTATION

In the case of water and salts the indications for parenteral administration are well known; they are most urgent when much water and salts are lost, for example in anhydremia (dehydration) from whatever

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1. Holt, L. E., Jr.; Tidwell, H. C., and Scott, T. F. M.: J. Pediat. **6**:151 (Feb.) 1935.
2. Burr, G. O., and Burr, M. M.: J. Biol. Chem. **82**: 345 (May) 1929.

cause. Serious symptoms may rapidly develop and death may ensue unless water and salts are given. Since some disease usually prevents oral assimilation, the essential water and salts must be given intravenously. If this is promptly done a rapid improvement in the clinical condition occurs, accompanied by a return of the chemical composition of the blood to normal.

The common indications for parenteral carbohydrate alimentation are likewise generally accepted. But what of the need for protein? As will be mentioned in more detail subsequently, this need should be discussed in terms of amino acid or nitrogen metabolism. Thus nitrogen in the form of amino acids is constantly needed to form new proteins, to take care of the wear and tear of tissue and for other purposes, even when abundant calories are supplied. Since there are great stores of protein in the muscle (and elsewhere) it has been generally assumed that, as long as calories are supplied, one need not be concerned about the need for nitrogen. The supposition has been that muscle, being a relatively nonvital tissue, can easily be spared to supply by hydrolysis the amino acids necessary for nitrogen metabolism even for long periods.

One of the first evidences that muscle or other nonvital protein stores become inadequate during protein starvation was the observation of hypoproteinemia, which often results in nutritional edema. Since serum protein becomes depleted it is inevitable that other sources of protein are similarly affected and that muscle therefore is not the only tissue which is being autolyzed. It then becomes important to know what clinical manifestations are produced when, for example, the liver protein reaches a low level. What occurs when the various endocrine glands and the cardiac muscle find their protein drawn on? These questions cannot be answered until more careful study is made of patients suffering from protein starvation. Its seems obvious, at any rate, that the skeletal muscle and liver (or any other more theoretical store of body protein) cannot always be depended on to satisfy nitrogen metabolism and that therefore the indications for parenteral protein alimentation are to that extent the same as those for carbohydrate. Briefly, they comprise conditions under which oral alimentation becomes defective or is contraindicated.

Oral alimentation fails in many circumstances besides the well known ones, e. g. when intestinal obstruction or repeated vomiting makes feeding impossible. Thus in cases of general peritonitis food can be given by mouth but only with deleterious results, even when vomiting does not occur. In cases of intestinal fistula or severe ulcerative colitis with diarrhea, food given by mouth may be either insufficiently digested or excreted before sufficient absorption can occur. Moreover, the hypermotility produced by the ingestion of food is said to be followed by an excessive loss of nitrogen in the urine and feces in many such cases. Intravenous alimentation not only supplies missing nutritional elements but permits the intestinal tract to be put completely at rest, a beneficial prerequisite to healing in many cases, especially when surgical procedures are necessary.

Perhaps the most clearcut indication for parenteral protein alimentation is the nutritional edema already mentioned, occurring because of hypoproteinemia. Especially important is the fact that the edema may involve the intestinal mucosa, interfere with absorption of food and lead to a vicious circle. In the past such intestinal edema was probably present at the stoma in many cases of pyloric obstruction in which obstructive signs persisted even after an adequate passage was produced by gastro-enterostomy. This proved puzzling to the surgeon and often led to further and useless operations. Recent studies, especially the experiments of Mecray, Barden and Ravdin,[3] have shown in fact that with the relief of hypoproteinemia both the edema and the obstructive manifestations disappear. Some type of parenteral protein alimentation is obviously essential in such cases, at least for a short time, in order to break the vicious circle; transfusions have been especially recommended in order to bring the serum protein content to normal.

Plasma as a source of intravenous protein alimentation can maintain nitrogen balance; this has been demonstrated experimentally.[4] As a source of nitrogenous nourishment it has certain practical drawbacks. Thus it would be necessary to give two 500 cc. transfusions a day in order to introduce 35 Gm. of serum protein, an amount which is certainly at the lower level of the protein needs of a 70 Kg. adult. Since the red cells are not needed, plasma should be separated from whole blood and given alone. A more serious defect in the use of plasma as a source of nitrogen nutrition is the fact that it supplies only one of the protein needs, i. e., the need for serum protein. In order to supply other tissues the protein must be first hydrolyzed by the body to amino acids, which then circulate in the blood and supply the various tissues, as illustrated in the accompanying chart. In a very sick patient this process may occur too slowly or perhaps not at all. This may be the reason that a transfusion for severe nutritional edema is sometimes ineffective (cases 2 and 8).

The indications for intravenous alimentation, finally, may become extended as more is learned about the various defects which occur in intestinal absorption. One example, due to hypoproteinemia, has already been mentioned. Recent observations by Groen [5] have shown a diminished intestinal absorption of dextrose in various deficiency diseases. Protein has many more hurdles to hop before it becomes available to the tissues. If digestion is defective or if absorption is impaired, an adequate supply of amino acids may not reach the tissues. The element of time may also be important; evidence will be presented subsequently [5a] suggesting that unless all the essential amino acids are present in the tissues at the same time synthesis may be impaired.

AMINO ACIDS FOR INTRAVENOUS PROTEIN ALIMENTATION

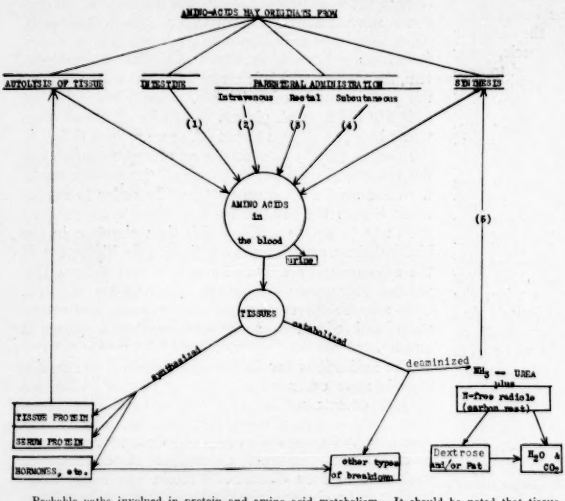
Protein as a source of parenteral alimentation can be given only in the form of amino acids, aside of course from the use of matched blood in a transfusion (or plasma alone), which has already been discussed. Amino acids represent the form in which protein food enters the blood stream from the intestinal tract after appropriate digestion and absorption; thus it has become customary to speak of the use of protein in terms of amino acid metabolism. Indeed, one may even speak of protein and amino acids in terms of nitrogen metab-

3. Mecray, P. M., Jr.; Barden, R. P., and Ravdin, I. S.: Surgery **1**: 53 (Jan.) 1937.
4. Holman, R. L.; Mahoney, E. B., and Whipple, G. H.: J. Exper. Med. **59**: 269 (March) 1934.
5. Groen, Julia: New England J. Med. **218**: 247 (Feb. 10) 1938.
5a. Elman, Robert: Proc. Soc. Exper. Biol. & Med., to be published.

olism, as nitrogen metabolism can be maintained by the administration of an adequate supply of protein or amino acids of the right sort. Since amino acids in general are soluble and nontoxic (in ordinary amounts) they should be just as suitable for intravenous injection as dextrose.

Of the twenty-one or more amino acids which make up the usual protein foods, only nine (possibly ten) are essential.[6] Thus by supplying an adequate amount of these nine amino acids the nitrogenous needs of the body should be met. This has been done [7] for growing rats; undoubtedly it would also suffice for the less rigorous needs of maintenance. From the practical point of view, however, such an approach is unfeasible because of the high cost of pure amino acids. A much more economical method is to hydrolyze protein after hydrolysis would have the same composition. Quantitative analysis of the amino acids in such a mixture would be valuable in revealing its deficiencies, but it is hampered at present by the lack of satisfactory methods for the estimation of all the amino acids. For these reasons a simpler approach is to test the biologic maintenance value of a particular mixture of amino acids by direct experiment. One method is based on studies of nitrogen balance; another is based on the regeneration of serum protein, the only bodily protein which can be more or less readily and directly measured. Both methods were used in the present observations.

Previous observations on parenteral alimentation with amino acids are few, aside from the many experiments in which single injections were made for chemical studies, such as those of Van Slyke and Meyer,[8] who injected protein hydrolysates into anesthetized dogs and studied the distribution of the amino acids several hours later. Henrique and Andersen [9] carried out intravenous alimentation for one month on a single goat; they used digested meats as their source of nitrogen. The animal remained in nitrogen balance and gained weight. Rectal alimentation with hydrolyzed protein was described by Abderhalden, Frank and Schittenhelm [10] and later by Griesbach.[11] Their patients showed definite evidence of utilization. The cases herein reported are believed to be the first in which hydrolyzed protein has been injected intravenously into human beings.



Probable paths involved in protein and amino acid metabolism. It should be noted that tissue protein and serum protein are not interchangeable directly; they must first be autolyzed and their amino acid constituents made available by the blood stream for synthesis by other tissues or cells. The numbers refer to the following considerations: 1. The amino acids from digested protein in the intestine are absorbed and enter the portal system slowly and at various rates, and they reach the liver before the muscle. 2. In contrast, by the intravenous route all amino acids reach the tissues at the same time; the liver receives them simultaneously with the muscle. 3. Rectal alimentation is subject to the vagaries of colonic absorption, which apparently varies considerably. 4. Subcutaneous alimentation requires large volumes of solution, since isotonicity must be maintained; when edema is present absorption may be delayed. 5. This mode of amino acid synthesis is based partly on theoretical considerations; it probably occurs, at least as far as the simpler amino acids are concerned, by a combination of ammonia and lactic acid or pyruvic acid (Sherman, H. C.: Chemistry of Food and Nutrition, ed. 5, New York, Macmillan Company, 1937, pp. 223-224).

a relative pure protein until it is broken down into its constituent amino acids. If the protein selected contains all the essential amino acids in adequate proportions, the resulting product should be suitable, provided of course that none of the essential constituents are destroyed during the process. Obviously also such a hydrolysate must prove entirely nontoxic when given intravenously in ordinary amounts. Although Rose has determined the ideal formula of essential amino acids for growth,[7] it is unlikely that any easily available

6. Most of our recent knowledge of the nutritive significance of amino acids has been contributed by the extensive researches of W. C. Rose and his collaborators. Much of this data as well as an able review of the literature can be found in two recent papers by this author (Science **86**: 298 [Oct. 1] 1937; Physiol. Rev. **18**: 109 [Jan.] 1938).

7. Rose, W. C.: Science **86**: 298 (Oct. 1) 1937.

EXPERIMENTAL OBSERVATIONS

The amino acids used in all the studies herein described were obtained from the acid hydrolysis of casein.[12] All the essential amino acids of casein were presumably present except tryptophan, which is destroyed during the hydrolysis. To make the mixture complete 2 per cent of this essential amino acid was added. Under these conditions the product supported normal growth in rats.[13] In many of our experiments 2 per cent of cystine (or methionine) was also added because of the low concentration of cystine in casein. The basic product (hereinafter called the incomplete mixture) without the added amino acids served excellently as a control in many experiments. Adult dogs were used exclusively. Chemical determinations were carefully checked by frequent duplicate analyses. In most experiments a macro-Kjeldahl method was used in determining nitrogen; in some, however, nesslerization was employed.

8. Van Slyke, D. D., and Meyer, G. M.: J. Biol. Chem. **16**: 197, 1913.

9. Henrique, V., and Andersen, A. C.: Ztschr. f. physiol. Chem. **88**: 357, 1913.

10. Abderhalden, E.; Frank, F., and Schittenhelm, A.: Ztschr. f. physiol. Chem. **63**: 215, 1909.

11. Griesbach, W.: Klin. Wchnschr. **2**: 1926, 1922.

12. This product was supplied by Mead Johnson & Co., of Evansville, Ind. The added tryptophan, cystine and methionine were obtained from the Eastman Kodak Company.

13. Kemmerer, H. S.: Personal communication to the authors.

Preliminary studies showed that the product was not anaphylactogenic for guinea pigs. By either the Folin colorimetric or the Van Slyke titrimetric method, 95 per cent of its nitrogen was in the form of amino acids. The product was easily soluble as a 10 per cent solution which was acid in reaction (p_H 5 to 6) and amber in color. An equal concentration of dextrose was always added not only because of its caloric value but also because there is considerable evidence that the utilization of amino acids is enhanced by the presence of carbohydrate. The rate of intravenous injection was important; a 10 Kg. dog was likely to retch or vomit (sometimes with diarrhea) if more than 100 Mg. of amino acids a minute or 6 Gm. an hour was given, and considerable amounts of amino acids might be lost in the urine. However, this rate is very high; in most experiments only about 1 Gm. of amino acids was injected an hour. Regardless of the rate of injection, it was found that the amino acids left the blood stream with great speed after even large intravenous doses.[14] In order to determine whether they were utilized, two types of experiment were carried out.

Studies of Nitrogen Balance.—When amino acids enter the blood stream they are subject to three possible effects, as shown in the accompanying chart. They may be excreted in the urine as such; they may be deaminized (or broken down in other ways) and measured in the urine as nitrogen (largely urea and ammonia); they may be retained and synthesized. The first possibility was avoided by a slow rate of injection. Whether retention occurred was then evident by study of the nitrogen excretion. Such balance experiments showed that almost complete retention of the amino acid nitrogen occurred whenever the complete mixture of amino acids was injected; under these conditions immediate nitrogen balance was achieved. Such retention of nitrogen is supposed to mean actual synthesis. Ordinarily this assumption may not be justified because of the possibility that the retained amino acids may be simply stored as such and not synthesized into protein. For this reason a control experiment was carried out with the incomplete mixture of amino acids (tryptophan and cystine were not added). If the hydrolyzed casein was retained as such, the retention should have occurred whether or not a few milligrams of tryptophane and cystine was added. Yet in each experiment with the incomplete mixture, very slight retention occurred. Moreover, under such circumstances nitrogen balance was not achieved. The details of these experiments have been described elsewhere.[15]

In further experiments with the incomplete mixture of amino acids it was found that nitrogen balance was not achieved if the missing essential amino acids (tryptophan and cystine) were injected separately eight hours after the injection of the basic mixture.[5a] It seemed therefore that retention and utilization of a mixture of amino acids required not only all the essential amino acids but that they be present at the same time. Thus, when an incomplete mixture is injected, apparently deaminization occurs rapidly and, if the missing essential amino acids appear on the scene too late, retention (and synthesis) do not occur. This phenomenon if confirmed would explain the relative superiority of intravenous over oral alimentation of protein when intestinal function is defective, since in this case delays in absorption of essential amino acids may lead to excessive loss of nitrogen by deaminization. Peters and Van Slyke[16] have discussed observations showing that deaminization occurs soon after ingestion of protein; destruction of amino acids apparently does not wait until all the protein has been digested and absorbed. The present observations confirm this theory. Further observations are being made of this interesting phenomenon.

Regeneration of Serum Protein.—There are many experiments recorded in the literature on the regeneration of serum protein reduced either by repeated plasmapheresis or by a long-continued nonprotein diet. In the present experiments a simpler and shorter procedure was used. In fasting dogs a reduction in serum protein was produced by a severe hemorrhage. In the controls no regeneration occurred in six hours and but little in twenty-four hours. If amino acids were injected intravenously, however, definite evidence of an increase in serum protein was obtained within six hours. These experiments have been described elsewhere.[17]

In another series of observations hypoproteinemia was produced by a nonprotein diet similar to that described by Weech, Goettsch, and Reeves.[18] In many of the dogs obvious nutritional edema appeared; they all showed a fall in the level of serum protein, usually within a few weeks. After the intravenous injection of a complete mixture of amino acids there was striking diminution of the edema, often within a few hours and always in twenty-four hours. The serum protein changes were far less striking. Nevertheless, in several experiments definite alleviation of the hypoproteinemia was achieved as compared with controls in which an incomplete mixture was used.

Histologic Studies.—All dogs receiving amino acids intravenously were eventually examined post mortem. The liver and kidneys in no case showed any evidence of change referable to the injected amino acids, even when large or long-repeated doses had been given.

CLINICAL OBSERVATIONS

Our first concern in giving hydrolyzed casein to patients was, of course, the possibility of untoward reactions, even though none had occurred in dogs. At first small doses were injected; they produced no demonstrable effect, so that eventually we administered what was thought to be a full daily quota of amino acids, i. e., from 0.5 to 2 Gm. per kilogram of body weight.

The hydrolyzed casein was generally made up as a 10 per cent solution and tryptophan and methionine (or cystine) added. It was then passed through a sterile Seitz filter and poured directly into 5 or 10 per cent dextrose solution as ordinarily prepared for routine use. In this way sterility was achieved without the danger of breaking up any of the amino acids through autoclaving. Usually each liter contained about 20 Gm. of amino acids to 80 Gm. of dextrose. If given slowly over the course of at least two hours the 20 Gm. of amino acids did not spill over into the urine and produced no objective reaction; there was no elevation

14. Elman, Robert: Proc. Soc. Exper. Biol. & Med. **37**: 437 (Dec.) 1937.
15. Elman, Robert: Proc. Soc. Exper. Biol. & Med. **37**: 610 (Jan.) 1938.
16. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams and Wilkins Company, 1931, vol. 1, p. 394.
17. Elman, Robert: Proc. Soc. Exper. Biol. & Med. **36**: 867 (June) 1937.
18. Weech, A. A.; Goettsch, E., and Reeves, E. B.: J. Exper. Med. **61**: 299 (March) 1935.

of temperature or pulse rate. Subjectively some patients noticed a sense of warmth, which was evident in a slight peripheral vasodilatation. One patient stated that he felt slightly chilly, but no chill occurred and the temperature remained normal; one child had a transient rash after one injection and vomited once.

About a score of patients were given amino acids intravenously, but to only eight were large amounts given for more than one or two days; their clinical summaries are given later. Complete chemical measurements were not carried out in many cases, so that the observations herein recorded are presented as preliminary studies. The results have been sufficiently promising to justify the hope that further use will produce added evidence that this method of alimentation not only is harmless but results in active and rapid synthesis of tissue and other protein. Both Kjeldahl and nesslerization methods were used in the determination of nitrogen. The albumin and globulin portions of serum were separated by Howe's method.

REPORT OF CASES

CASE 1.—W. C., a man aged 55, a patient at the St. Louis City Hospital, had an extensive inoperable carcinoma of the stomach, with complete obstruction at the cardia, so that he could ingest no nourishment and was rapidly deteriorating in spite of intravenous and subcutaneous administration of dextrose and saline solutions. For one month he received continuous venoclysis, consisting each day of 4,000 cc. of 10 per cent dextrose containing 20 Gm. of hydrolyzed casein with added tryptophan and cystine and 750 cc. of physiologic solution of sodium chloride. No reaction occurred and no subjective manifestations were apparent; the general condition, which was rapidly going downhill, was improved so that the patient seemed stronger and was able to read and smoke. The nitrogen output in the urine varied between 3 and 4 Gm. a day. Nitrogen balance was achieved whenever the dose of amino acids was increased to a point above this level. However, if tryptophan and cystine were omitted from the mixture the output of urinary nitrogen rose to 5 and 6 Gm. a day. The serum protein content at the beginning of the experiment was 4.31 Gm. per hundred cubic centimeters and at the end 5.52 Gm.; this increase was mostly in the albumin fraction, which rose from 2.35 to 3.16 Gm. per hundred cubic centimeters. That this increase was probably not due to concentration (decrease of plasma volume) was suggested by the red cell count, which remained at about 3,000,000 during the entire period.

CASE 2.—I. H., a man aged 51, a patient at the St. Louis City Hospital, after resection of the intestine for volvulus two months before had had a stormy course. When first seen he was emaciated and exhibited a pronounced nutritional edema in spite of fifteen transfusions. Although enterostomy had produced a functioning opening, frequent stools were passed; food was eaten, but obviously little if any was assimilated. The serum protein content was 3.54 Gm. per hundred cubic centimeters equally divided between albumin and globulin. On two successive days 500 cc. of blood was given without affecting the edema. A reaction followed one of the transfusions. Acacia was also given without effect. Nov. 16, 1937, 20 Gm. of amino acids was given in 750 cc. of 10 per cent dextrose solution without reaction. The following day the edema was definitely better, and 3,000 cc. of urine had been excreted; the patient stated that he felt better. There was no immediate change in the serum protein. On other occasions transfusions of whole blood as well as of plasma alone were given to this patient without influencing the edema; each time amino acids were injected a reduction of edema occurred. The serum protein value eventually rose to 5.01 Gm. per hundred cubic centimeters but fell again on cessation of intravenous alimentation, which finally became impossible because of thrombosis of the existing veins. The patient, who at all times was on the verge of nutritional collapse, finally died of pneumonia. It was felt that a shorter and more intensive regimen of dextrose and amino acids alone might have saved his life.

The influence of rapid changes in plasma volume on the concentration of serum protein was observed several times in this patient. On one morning the serum protein content was 4.29 Gm. per hundred cubic centimeters; in the evening, after intravenous administration of fluid, it was 3.11 Gm.; that this was due largely to dilution of the blood was shown by a fall in the hematocrit reading (cell volume) from 48 to 40 per cent and of the red cell count from 5.5 to 4.5 million. On another occasion the serum protein content fell from 4.06 to 3.51 Gm. after administration of fluids. Also the hematocrit reading (cell volume) fell from 50 to 40 per cent and the red cell count from 5.18 to 4.4 million.

CASE 3.—R. B., a woman aged 67, a patient at the St. Louis City Hospital, had an inoperable carcinoma of the stomach and could take nothing by mouth. Intravenous alimentation with dextrose and saline solutions was carried out until the urinary output of nitrogen reached a level of about 4 Gm. a day. On three successive days 4.5 Gm. of nitrogen as amino acids was added to the dextrose solution, only slightly increasing the output of nitrogen. It was concluded that almost complete retention of the injected amino acids occurred. No reaction whatever accompanied this experiment.

CASE 4.—W. W., a man aged 75, a patient at the St. Louis City Hospital, had an obstructing carcinoma of the esophagus but refused gastrostomy and agreed to intravenous alimentation. The nitrogen output of the urine was measured daily. When the complete mixture of amino acids with dextrose was injected, little change in nitrogen output occurred and the patient achieved nitrogen balance at once. When the incomplete mixture was used, a large increase in urinary nitrogen appeared, thus confirming for human beings the observations already mentioned for dogs. No reaction was observed after the injections. This patient showed wide variations in the concentration of serum protein, often but not always explainable by changes in plasma volume as revealed by the hematocrit.

CASE 5.—N. O., a woman aged 69, a patient at the St. Louis City Hospital, had severe septicemia and was comatose for most of her clinical course until she died. Because nutritional edema with hypoproteinemia developed, amino acids were added for three days to the intravenous drip of dextrose and saline solutions. The urinary output of nitrogen was level at about 4 Gm. a day. Although the daily quota of injected nitrogen as amino acids was 5.16 Gm., the urinary nitrogen increased only to 4.5 Gm., indicating achievement of a definitely positive nitrogen balance. The serum protein content increased from 4.89 to 6.06 Gm. during this period, while the hematocrit reading remained unchanged.

CASE 6.—R. P., a boy aged 8 months, a patient at the St. Louis Children's Hospital, who was in the hospital for two months before he died, entered with an infection of the upper part of the respiratory tract which required myringotomy and eventually bilateral mastoid antrostomy. There then developed severe persistent dysentery (Hiss-Russell), which failed to respond to any form of therapy. Many transfusions were given. The general condition grew steadily worse, and his weight fell from 6,200 to less than 4,500 Gm. At autopsy the only abnormality found was pronounced shaggy ulcerative colitis involving the entire colon.

At the suggestion of Dr. A. F. Hartmann a continuous intravenous drip was instituted; this was done during the most critical period of the baby's illness. For ten days 50 Gm. of dextrose and 10 Gm. of amino acids in 500 cc. of half strength Ringer's solution was given daily. Under this regimen the clinical condition of the baby improved, and the stools became less frequent and more nearly normal. Eventually all the veins were used, and no further venoclysis was possible. There was no evidence of reaction during the period of intravenous alimentation. Chemical studies of the blood showed a surprising fall in the concentration of serum protein from 4.76 to 3.53 Gm. per hundred cubic centimeters. However, the hematocrit reading (cell volume) fell even more, i. e., from 44 to 22 per cent, indicating a rise in the relative plasma volume and therefore an increase rather than a decrease in the total plasma

protein. The baby showed no edema in spite of the hypoproteinemia. Death occurred suddenly several days after the intravenous therapy had ended.

It is of interest to note that although this baby received over 2 Gm. of amino acids per kilogram of body weight a day for ten days, histologic study of the liver, kidney and spleen at autopsy revealed no changes.

CASE 7.—J. C., a boy aged 2 years, a patient at the St. Louis Children's Hospital, had chronic nephrosis with hypoproteinemia and edema. At the suggestion of Dr. A. F. Hartmann he was given intravenously each day for three days 15 Gm. of amino acids and 35 Gm. of dextrose in 350 cc. of Ringer's solution, divided in two equal doses, each injection lasting two hours. There was no reaction except that on the third day a transient macular rash developed and he vomited once. Study of the serum protein showed a slight increase, from 3.92 to 4.51 Gm. per hundred cubic centimeters, largely due to the albumin fraction, which increased from 1.5 to 1.88 Gm. The hematocrit reading (cell volume) during this period changed but little (34 to 36 per cent).

CASE 8.—C. T., a man aged 67, a patient at the Barnes Hospital, was seen in consultation with Dr. N. A. Womack, who suggested the use of amino acids. He was already emaciated when enterostomy was performed for intestinal obstruction. After operation severe nutritional edema developed. The serum protein content was first 4.9 Gm. per hundred cubic centimeters; in spite of a transfusion one week later it had fallen to 3.4 Gm. There was no corresponding change in the red cell count. Acacia was also used, but the edema increased and the general condition grew worse; vomiting and distention developed, requiring continuous gastric suction. Hypertonic sucrose solution was also used without apparent effect. Twice each day he had been receiving 1,000 cc. of 10 per cent dextrose intravenously; on four successive days amino acids were added to the dextrose, so that he received 40 Gm. of the hydrolyzed casein daily (the patient's weight was estimated at 40 Kg.). No reaction occurred, the only subjective sensation being a sense of warmth during the injection and once a feeling of momentary chilliness afterward. Twenty-four hours after the start of the injections a definite decrease in the edema was obvious; this improvement continued until the edema was entirely gone several days later. Vomiting ceased, and the patient started to eat. There was definite diuresis; much fluid was also lost through the enterostomy opening. The general condition improved, and bowel movements soon appeared by rectum. The serum protein content rose to 3.9 and then to 4.7 Gm. per hundred cubic centimeters several days after cessation of the intravenous therapy. The red cell count remained constant at about 3.9 million, suggesting that there was no change in relative plasma volume.

All patients coming to autopsy were especially examined for any parenchymatous changes in the liver or kidney which might be indicative of a toxic effect of the injected amino acids. No such evidence was found. This was especially significant in case 6, in which over 2 Gm. per kilogram a day had been given for ten consecutive days.

COMMENT

Only a few of the many aspects of intravenous alimentation have been considered in the present paper. The observations recorded, however, seem to indicate that the nitrogen needs of the body can be supplied by the intravenous administration of an appropriate mixture of amino acids. Such a mixture can be prepared by the acid hydrolysis of casein; it was given intravenously to dogs and to human beings with no evidence of toxic reaction either clinically or anatomically. Unfortunately such a product lacks tryptophan, which must be added before the mixture will support nitrogen metabolism; this is an important defect from the practical point of view, because tryptophan is one of the most expensive of the many amino acids. Other preparations of hydrolyzed protein are now being studied. It is probable that a complete as well as inexpensive mixture will soon become available for clinical trial.

The experimental and clinical results herein presented constitute definite evidence that the injected amino acids are actually utilized by the body to supply its nitrogen needs. Much of this evidence consists of observations on nitrogen balance. Although these studies involve the assumption that retention of the injected amino acids means synthesis, control experiments tended to justify this assumption. The most dramatic effect of the injection of amino acids occurred in the relief of nutritional edema and in the apparent improvement in the general condition of several very sick patients. There was, it is true, an occasional failure to correlate these clinical effects with a prompt elevation of the serum protein content. It should be stated, however, that in many studies of hypoproteinemia by others considerable lag has been noted between the appearance (and disappearance) of nutritional edema and the changes in the serum protein. This lack of exact parallelism between serum protein concentration and nutritional edema may be due to other factors which influence edema; retention of salt immediately comes to mind. In the present study salt edema was not present. One must also consider the effect of rapid changes in the plasma volume on the serum protein concentration, which is especially shown in case 2. On the other hand, when a rapid fall in serum protein content was produced by a severe hemorrhage, definite evidence of regeneration was observed to follow rapidly the administration of amino acids.[17]

With regard to the quantity of dextrose and amino acids needed for intravenous alimentation, a rough estimate should be made. For a 70 Kg. adult certainly 1,600 calories should be given, and more if fever is present. Thus at least 400 Gm. of dextrose and amino acids should be injected. Of the latter, sufficient should be given to keep the patient in positive nitrogen balance. From the various statements in the literature at least 0.5 Gm. per kilogram should be adequate. In the adult patients observed by us in which the excretion of nitrogen was studied for a long period, 5 Gm. a day was the usual maximum output. This corresponds to an amino acid intake of over 30 Gm., which is just about the 0.5 Gm. per kilogram just mentioned. In other patients the nitrogen needs are probably much greater. Ringer's solution meets the need for electrolyte, though a note of warning should be uttered with regard to the danger of giving too much salt. Ordinarily from 7 to 10 Gm. of sodium chloride a day should be sufficient. If this amount is exceeded, the kidneys may not be able to excrete all of it and retention of salt may follow; this salt may gather in the tissues and rapidly produce a salt edema. One liter of physiologic solution of sodium chloride (or Ringer's solution) is usually ample, except of course in the case of anhydremia, when much more is required at the beginning at least to relieve the hypochloremia.

The remaining requirements for complete intravenous alimentation, namely vitamins and fat, obviously call for extensive study. Doubtless in a few patients utilization of dextrose and amino acids is impaired because of missing vitamins. These accessory food factors are much more than antidisease substances; their primary effects are metabolic and are even now being carefully

studied by many workers. It may be that most patients in whom intravenous alimentation is indicated do not have significant vitamin deficiency, so that for them the injection of these food factors is not needed. As for fat, it seems likely that for maintenance it may be dispensed with. On the other hand, from the practical point of view fat has a great advantage in parenteral alimentation. The mechanical problem of injecting enough calories would be simplified by the availability of fat, since it produces two and one-half times as many calories per gram as dextrose or amino acids.

SUMMARY

For the first time, it is believed, a mixture of amino acids has been given intravenously to human beings for parenteral protein alimentation. The mixture was obtained by the acid hydrolysis of casein to which was added 2 per cent tryptophan and cystine (or methionine). No evidence of toxicity either clinically or histologically was observed when the injection was given slowly, even though as much as 2 Gm. per kilogram a day was injected. Experimental and clinical observations have indicated that the injected amino acids are rapidly utilized; this was shown by nitrogen balance studies, by regeneration of serum protein and by reduction of nutritional edema.

ABSTRACT OF DISCUSSION

DR. THEODORE L. ALTHAUSEN, San Francisco: I didn't intend to discuss the work of Drs. Elman and Weiner, but a paper which offers something new should not go without discussion. After intravenous administration of dextrose came into general use, various investigators began to cast about for means of similarly administering fats and proteins, especially in cases in which parenteral alimentation has to be carried on for longer periods. Dr. Emmett Holt Jr. devised a successful method of administering intravenously emulsions of fat to children. Another investigator has experimentally used protein hydrolysates for nutrient enemas with apparent success. The authors are the first to come out officially with their work in the field of parenteral administration of amino acids. From my own work I am very much interested in the important part which dextrose plays in the metabolism of fats and in practical application of this, for instance in the treatment of ketosis. It was interesting to hear that dextrose is also necessary for the utilization of amino acids.

DR. THOMAS T. MACKIE, New York: The development of a nutritionally complete diet which may be administered intravenously would constitute an exceedingly important contribution to the therapy of many conditions. Present limitations of parenteral and intrarectal feeding inevitably induce malnutrition if continued for more than brief periods. This in its turn implies an added hazard to the patient. If further studies confirm the authors' preliminary results this work may constitute one of the most important contributions to therapy of recent years.

Servetus.—It was in 1546 that Servetus discovered the lesser circulation of the blood. Cesalpinus (1524-1603) discovered the greater circulation in 1569; and Sylvius (1478-1555) and Fabricius of Aquapendente (1537-1619) discovered the valves in the veins before 1574, thus antedating even the birth of Harvey by four years. Servetus, in his book on the "Trinity," had fearlessly announced that Galen was wrong in his ideas of the circulation of the blood. He showed for the first time that there was no communication between the two sides of the heart, and that the blood flowed from its right side to the lungs, and returned to its left side to be sent to all parts of the body. Harvey, who somewhat later studied in Italy and France, also knew these facts; but he dared not publish them in England during the reign of his kings, James I and Charles I.—Hurd-Mead, Kate Campbell: A History of Women in Medicine, Haddam Press, 1938.

CHRONIC ADHESIVE SPINAL ARACHNOIDITIS

A CLINICAL AND PATHOLOGIC STUDY

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CHICAGO

Chronic fibrotic or adhesive changes in the spinal arachnoid have been described for more than forty years. Designated as meningitis, or more often as arachnoiditis, these changes have been characterized as serous, fibrous, adhesive or cystic and as diffuse, disseminated or circumscribed. The first report was that of Schwarz,[1] who in 1897 described the clinical and pathologic features in a case supposedly of syphilitic origin, with sclerotic and cystic meninges and focal areas of softening and cavitation in the spinal cord. Schwarz's article is one of the few containing detailed pathologic descriptions and has never received the attention it deserves. Circumscribed cysts of the arachnoid are especially apt to simulate tumors, as shown in the first report from America, in 1903, by Spiller.[2] Numerous later reports, such as those by Horsley,[3] Munro,[4] Schuster,[5] Mauss and Krüger,[6] Stookey,[7] Barré,[8] Elkington,[9] and Selinsky[10] and particularly the extensive monographs by Metzger[11] and Paulian and Turnesco,[12] contributed to our clinical knowledge of the various types of spinal arachnoiditis without, however, completely solving the diagnostic difficulty. Even today the condition is rarely differentiated preoperatively from cord tumor if a manometric block is present, and if a block is absent the disease is often missed entirely and left buried in such doubtful clinical categories as "lateral sclerosis" or "paraplegic multiple sclerosis." In some cases it is mistaken for subacute combined degeneration of the cord and in others for amyotrophic lateral sclerosis.

The pathologic characteristics of spinal arachnoiditis have been described by a few workers, but chiefly with regard to the state of the arachnoid rather than the cord. Schwarz's report,[1] the first, is one of the best. Horsley[3] gave brief descriptions of the gross changes, pointing out the tendency toward degeneration of the white matter around the margins of the spinal cord underlying the pia. The pathologic studies of Schuster,[5]

From the Research and Educational Hospital of the University of Illinois and St. Luke's Hospital.

Read before the Section on Nervous and Mental Diseases at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

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Gerstmann,[13] Bonhoeffer,[14] Pette,[15] Harbitz and Lossius,[16] Brouwer,[17] Marinesco and his associates[18] and Yasuda[19] have added much to our knowledge of the alterations in the spinal cord. None of this pathologic study on the cord has been done in America, and little of the literature is available in English. Grinker's[20] observations were made in a case in which the spinal cord was largely spared.

ARACHNOIDITIS FOLLOWING ACUTE MENINGITIS

CASE 1.—*Acute (meningococcic?) meningitis followed after five weeks by generalized pains, paraplegia with muscular twitches, painful spasms and atrophy, unequal reflexes, extensor plantar responses and subarachnoid spinal block; operation; death; chronic adhesive arachnoiditis with extensive focal softening of the cord.*

History and Examination.—L. S., an unmarried white man aged 24, a laborer, was admitted to the service of Dr. LeRoy Sloan at the Illinois Central Hospital, Chicago, Sept. 28, 1934. Three years previously an attack of acute otitis media had subsided after parcentesis. Beginning August 15 he was critically ill for five weeks with a purulent form of meningitis in which no organism could be identified in the small hospital where he was a patient. Treatment included only symptomatic measures and frequent spinal punctures. Although his general condition improved, weakness of the lower extremities with urinary incontinence appeared soon and grew progressively worse. Headache persisted and pains appeared in the neck, back and legs, with transient attacks of "numbness" in the arms.

Examination on admission in the sixth week of illness revealed extreme flaccid weakness of the lower extremities including the flexors of the hips. Gross fascicular muscle twitches were seen in the thighs and calves. Superficial sensibility was normal except for a small perianal area of hypesthesia and somewhat delayed responses below the umbilicus. Vibration and position sense was abolished in the lower extremities. In the right leg the tendon reflexes were exaggerated; in the left, the patellar and internal hamstring reflexes were absent, while the achilles and external hamstring reflexes were reduced. The abdominal reflexes were normal, but the Babinski response was strong on both sides. There was urinary and fecal incontinence.

Lumbar puncture produced only one drop of yellow viscid fluid, but cisternal puncture revealed normal fluid with normal dynamic responses. Iodized oil introduced into the cisterna magna was arrested in irregular masses scattered between the first and fourth cervical vertebrae. Roentgen examination of the mastoids and lungs gave negative results; the sputum contained numerous leukocytes and pneumococci; Wassermann and Kahn tests of the blood and cisternal fluid were negative. The urine was normal except for many erythrocytes, a few leukocytes and a trace of albumin.

Course.—The patient's temperature and pulse remained normal, but headache and pains in the neck, back and extremities persisted. Gradually some weakness appeared in the arms and a small decubitus ulcer over the sacrum.

Operation.—At St. Luke's Hospital, October 23, Dr. Eric Oldberg performed a midcervical laminectomy and found a greatly thickened dura and an exceedingly dense, vascular arachnoid membrane which was adherent to the cord. Some of the adhesions were broken up, the iodized oil was aspirated, and the wound was closed.

Postoperative Course.—Troublesome headache and pains in the spine and extremities persisted. Motor weakness increased in all extremities, and painful muscle spasms began. Atrophy appeared in the shoulders, arms and legs and advanced slowly. Priapism and urinary and fecal incontinence were distressing. Superficial sensibility was but little disturbed but vibration and joint sense remained absent in the lower extremities. Death occurred December 3 of respiratory failure.

Autopsy.—Postmortem examination, done in the department of Dr. H. Gideon Wells of the University of Chicago, revealed marked generalized emaciation, pressure necrosis over the sacrum, hemorrhagic cystitis with hypertrophy of the urinary bladder and multiple renal abscesses. There was also questionable early bronchopneumonia.

Gross examination of the nervous system disclosed a few meningeal adhesions over the base of the brain and diffuse meningeal fibrosis throughout the spinal canal. In the cervical and lumbar regions numerous small cystic cavities were found in the subarachnoid space, filled with a gelatinous substance, but in the thoracic region a simple dense fibrosis surrounded the cord.

Microscopically the meninges were the seat of a diffuse chronic inflammatory process, with infiltration by lymphocytes

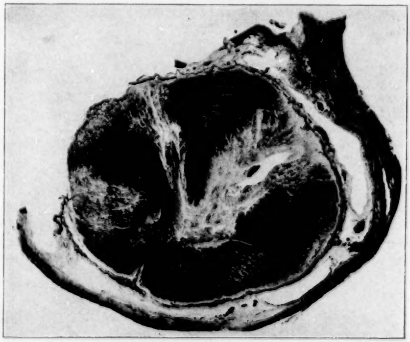

Fig. 1 (case 1).—Fibrosis, infiltration and cyst formation in the leptomeninges; secondary degeneration in the fasciculus gracilis; focal softening with demyelinization, especially in the periphery of the white matter, and degeneration of the gray substance with cavitation. Weigert-Pal stain, counterstained with van Gieson stain; reduced from a photomicrograph with a magnification of 8 diameters.

and plasma cells and marked collagenous fibrosis (fig. 1). No polymorphonuclear leukocytes or bacteria were found. These hyperplastic meninges were very vascular and the numerous vessels showed intimal and medial thickening, with occasional occlusion and hyalinization (fig. 2). Normal vessels were few. In many areas cystic cavities were found in the meshes of the fibrosed arachnoid, but none were large enough to have produced compression of the spinal cord. These cavities were lined by flattened or cuboidal epithelial cells, which were heaped up into several layers in some localities (fig. 3). Spinal nerve roots passing through these inflamed tissues were often remarkably free of changes, but some, particularly dorsal roots, were definitely degenerating and exhibited hyperplasia of the endoneurium.

The spinal cord itself showed extensive changes. In Weigert-Pal preparations the dorsal columns exhibited secondary or wallerian degeneration, due to the destruction of the dorsal roots by the inflammation and sclerosis in the meninges (fig. 1). In the cervical segments this process was almost restricted to the fasciculus gracilis. Scarlet red stains showed great amounts of fat in this region, most of them lying free in the tissues.

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Moderate astrocytic gliosis was found in the dorsal columns, proportionate to the degree of degeneration.

The most striking changes in the spinal cord, however, were the focal areas of softening which occurred in both white and gray matter. In the myelin sheath stains, any portion of the white substance seemed liable to this focal destruction, but the marginal or subpial regions were especially affected (fig. 1). In this manner the randdegeneration of the German observers was presented. Where necrosis was severe, all tissue elements had suffered, both parenchymatous and glial, and scarlet red stains revealed enormous amounts of fat lying free in the tissues. In the less acutely degenerated regions, there was reactive astrocytic gliosis. Numerous fat-granule (gitter) cells were found under the pia and about blood vessels.

In many areas the gray matter had undergone almost complete liquefaction with cavitation (fig. 1). There was no tissue response, glial or collagenous, in such regions. In other localities the gray matter was less severely involved, but the ventral horn cells were sharply reduced in number. The remaining ganglion cells were deformed, shrunken and hyperchromatic, or swollen and chromatolytic, with eccentric, pale nuclei (fig. 4). Such cells were studded with fat droplets when suitably stained. Satellitosis and neuronophagia were strikingly absent, however.

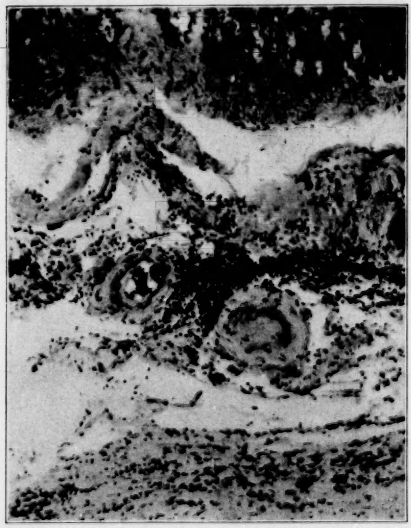

Fig. 2 (case 1).—Fibrosis and mononuclear infiltration in the leptomeninges; thickening of vascular walls with occlusion; status spongiosus in white matter. Weigert-Pal and van Gieson stains; slightly reduced from a photomicrograph with a magnification of 160 diameters.

Blood vessel walls in the areas of focal necrosis were thickened in all three layers and the lumen sometimes obliterated. Round cell infiltration was occasionally seen about these vessels. Compensatory formation of new vessels led to increased vascularity throughout the whole cord.

Emphasis from a clinical standpoint in this case should be placed on the purulent, possibly meningococcic, meningitis, which gradually gave place to progressive paraplegia with widely disseminated "root pains," paresthesias, painful involuntary muscle spasms, eventually disseminated atrophy and loss of deep sensibility but relative preservation of superficial sensibility. The spinal subarachnoid block and characteristic arrest of iodized oil at multiple levels clinched the diagnosis. The unsatisfactory surgical results were due to the impossibility of attacking so intense and diffuse a process. The most significant pathologic features were (1) the intense fibrosis and vascularization of the arachnoid, with the formation of arachnoid cysts lined with epithelium, (2) the tendency to vascular thickening and occlusion in both the pia-arachnoid and spinal cord and (3) the focal softening of both the white and the gray matter of the cord. One cannot speak here of a myelitis secondary to the meningitis, since evidences of inflammation in the cord were practically absent. It was rather a gradual process of ischemic necrosis.

CASE 2.—F. S., a white woman aged 45, experienced sudden and complete paraplegia in February 1935. There was a history of "influenza and meningitis" without spinal puncture in 1918, an illness from which she apparently recovered except for occasional back pains during the intervening sixteen years. Examination revealed paralysis with atrophy in the lower extremities and anesthesia below the first lumbar dermatome. The patellar reflexes were absent, the achilles exaggerated bilaterally. Spinal puncture revealed a complete block and 1,310 mg. of total protein per hundred cubic centimeters of spinal fluid. Disregard of the history of meningitis led to a mistaken diagnosis of spinal cord tumor. At operation Dr. Eric Oldberg found an opaque, densely fibrotic and vascular arachnoid membrane which was impregnated with large calcified flakes (fig. 5). Surgical attack was not possible. A year and a half later no improvement had occurred, and severe back pains persisted. In this case the sudden onset of paraplegia was probably due to vascular occlusion in the cord.

CASE 3.—E. P., a Negro girl aged 13, had had acute meningitis of unknown type when 21 months old. Five years later she had begun to have severe disseminated root pains and progressive spastic paraplegia with atrophy. Examination revealed in addition irregular sensory disturbances below the first thoracic dermatome, with a tendency to dissociation of pain and temperature senses. There were complete spinal block and scattered arrest of iodized oil at the third cervical and fourth and fifth thoracic vertebrae. At operation Dr. Eric Oldberg found a greatly thickened, opaque and vascularized arachnoid membrane, with two elongated arachnoid cysts. There had been no improvement two and one-half years later.

ARACHNOIDITIS ARISING SPONTANEOUSLY

CASE 4.—*Disseminated pains, paresthesias and progressive spastic paraplegia for three years; minimal superficial sensory loss; no spinal block; operation; death; advanced fibrosis and vascularization of arachnoid, with focal softening of cord.*

Clinical Abstract.—Mrs. G. B., a white woman aged 40, gave a history in March 1932 of disseminated pains, paresthesias and progressive weakness in the lower extremities for three years without significant antecedent phenomena. Examination revealed marked spastic paraplegia with only slightly diminished superficial sensibility but greatly reduced vibration and position sense in the lower extremities. The Babinski response was present on both sides. Painful spasms occurred in both legs. There was no block of the spinal fluid, the protein content was normal and the gold curve 2223221000. The spinal fluid Wassermann reaction was negative. At operation, Feb. 20, 1933, Dr. Eric Oldberg found the spinal arachnoid opaque, tough and vascular, and adherent to the cord. Nevertheless, much of the membrane was dissected free. The patient's condition failed to improve and she died of an infection of the operative wound on the twenty-sixth day after operation.

Autopsy.—The whole spinal arachnoid was thick and fibrotic and there were multiple foci of degeneration in the cord. Microscopically the arachnoid membrane consisted of almost solid collagenous connective tissue with no definite cystic areas and no infiltration except for occasional small mononuclear cells (fig. 6). The fibrotic meninges were markedly vascularized and the vessel walls thickened, often to complete occlusion of the lumen. The endothelial lining of the subarachnoid spaces

was hyperplastic wherever not overrun by fibrous tissue. Some of the spinal roots traversing the sclerotic meninges showed degeneration of both myelin and axis cylinders, with proliferation of the endoneurium.

In the spinal cord (fig. 6) there was secondary degeneration of the fasciculus gracilis with marked reactive gliosis. In addition there was subpial degeneration leading at some levels to status spongiosus around the periphery of the section. Focal areas of degeneration were scattered elsewhere throughout the cord and varied in diameter from less than a millimeter to half the cross section of the cord. Some of these were old and gliotic; others were areas of recent softening, with equal degeneration of glia and white and gray parenchyma, without noticeable reaction. Ganglion cells in these regions had disappeared or degenerated without satellitosis or neuronophagia. Some were small and hyperchromatic, others swollen and pale with eccentric or broken-down nuclei. There was no cavitation or liquefaction. Blood vessels in the cord, like those in the meninges, were increased in number and their walls thickened, sometimes with occlusion of the lumen. There was no perivascular infiltration, but small recent hemorrhages were occasionally seen.

The clinical differences between this and the preceding cases lie in the absence of any history of antecedent acute meningitis and in the absence of signs of subarachnoid block. In other respects the syndrome was almost identical in all four cases. Pathologically, the resemblance to the appearances in case 1 is extremely close.

CASE 5.—A. D., a white man aged 39, fell and injured his right shoulder and knee in January 1932, with subsequent paresthesias for a few days in the lower extremities, followed by progressive paraplegia, both sharp and aching leg pains, painful leg cramps, and eventually incontinence of urine and feces. Examination in May 1932 revealed advanced spastic paraplegia without atrophy or fibrillation. Abdominal reflexes were absent and the Babinski reaction was positive on both sides. All forms of sensation were normal. There was no subarachnoid block but the spinal fluid contained 56 mg. of total protein per hundred cubic centimeters. Evidences of old

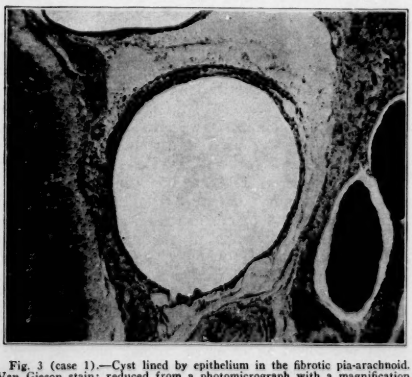

Fig. 3 (case 1).—Cyst lined by epithelium in the fibrotic pia-arachnoid. Van Gieson stain; reduced from a photomicrograph with a magnification of 60 diameters.

spondylitis were seen in roentgenograms of the spine. At operation, May 21, 1932, Dr. Eric Oldberg found a thick, tough arachnoid membrane, adherent to the spinal cord. A few adhesions were broken down. Six months later, weakness and atrophy were found in the left hand. Five years later he had greatly improved but still had a spastic gait, a positive Babinski reaction on both sides, and normal spinal fluid without a block. The achilles reflexes were now absent.

There is a suggestion that trauma may have played a part in this case. No history of meningitis was present. Again, as in case 4, no subarachnoid block was present. The diagnostic features consisted of the diffuse paresthesias and pains with cramps, the eventual presence of atrophy in the hands and the loss of the

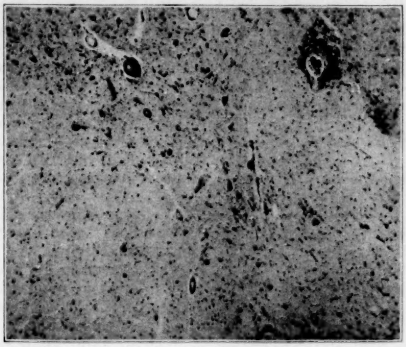

Fig. 4 (case 1).—Ventral horn, with destruction of many ganglion cells and pyknosis of others; note proliferation of adventitia and hemorrhage about vessels. Toluidine blue; reduced from a photomicrograph with a magnification of 60 diameters.

previously exaggerated achilles reflexes. In this case alone, of the five reported, operation was followed by improvement.

COMMENT

Etiology.—In three of the five cases reported the arachnoiditis appeared to result from some form of acute meningitis. The organism was probably the meningococcus, although such an opinion is hypothetic. In the last two cases the condition arose apparently de novo, a circumstance often recorded in the literature. In general the literature on the etiology of chronic adhesive spinal arachnoiditis indicates three possibilities. The first is infection, which may be meningococcic,[21] pyogenic,[22] syphilitic,[23] influenzal,[24] gonorrheal,[25] herpetic,[26] typhoid[27] or even tuberculous.[13] Cases have been reported of arachnoiditis following

21. Batten, F. E.: Paraplegia Following Cerebrospinal Meningitis: Laminectomy, Proc. Roy. Soc. Med. (Neurol. Sect.) **9:** 63 (March 30) 1916. Barré, J. A; Leriche, R., and Morin, P.: Troubles radiculo-médullaires par arachnoidite feutrée et kystique de la région dorsale, Rev. neurol. **32:**604-618 (May) 1925. Schaeffer, Henri, and de Martel, T.: Arachnoidite spinale circonscrite: Intervention opératoire; Guérison, ibid. **37:** 413-420 (March) 1930. Guillain, Georges, and Sigwald, J.: Arachnoidites spinales consécutives à la méningite cérébrospinale à meningocoque, ibid. **39:** 516-521 (March) 1932. Elkington.[9] Brouwer.[12]

22. Roger, Henri, and Alliez, Joseph: Dix cas d'arachnoidite spinale, aiguë ou subaiguë, kystique ou feutrée, primitive ou secondaire, Rev. neurol. **40:** 974-983 (June) 1933.

23. Pette, H.: Weitere klinische und pathologisch-anatomische Beiträge zum Kapitel der Frühlues des Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **92:** 346-378, 1924. Clarke, Norman E.: Loculated Meningitis with the Syndrome of Froin in the Spinal Fluid, Arch. Neurol. & Psychiat. **12:** 173-186 (Aug.) 1924. Alajouanine, T.; Hornet, T., and André, A.: Le feutrage arachnoidien postérieur dans les lésions syphilitique de la moelle (tabes, sclérose combinée, myélite), Rev. neurol. **65:** 266-276 (Feb.) 1936. Schwarz.[3] Munro.[4] Elkington.[9]

24. Vincent, Clovis; Peuch, Pierre, and David, Marcel: Sur le diagnostic, le traitement chirurgical, le prognostic des arachnoidites spinales, Rev. neurol. **37:** 577-595 (April) 1930. Kikuchi, Iwao: Nachtrag von drei Fällen der mit Laminectomie ganz erfolgreich behandelten Meningitis spinalis circumscripta chronica, Ztschr. d. japan. chirurg. Gesellsch. **36:** 126-127, 1935. Horsley.[8] Brouwer.[12]

25. Horsley.[8] Elkington.[9]

26. Paulian, D.; Demetrescu, J. R., and Cardas: Zona et arachnoïdite, Bull. et mém. Soc. méd. d. hôp. de Paris **1:** 255-258 (Feb. 16) 1934. Romay, Ramon Soto, and Dassen, Rodolfo: Meningo-radiculo-neuritis y aracnoiditis espinal fibro-adhesiva y quistica zosteriana, Semana méd. **44:** 663-669 (March 4) 1937.

27. Urechia and Jacobovici: Sur quelques cas d'arachnoïdite spinale, Paris méd. **2:** 145-148 (Aug. 12) 1933.

so-called lymphocytic meningitis [28] and various forms of meningomyelo-encephalitis. In an article on the latter disease, Biemond [29] has contributed from Brouwer's clinic an interesting pathologic description of an acute form of meningomyelitis with extensive inflammatory and necrotic changes in the cord. The second etiologic possibility is trauma, of which numerous examples have been recorded.[30] Mauss and Krüger [6] recorded twenty-three cases of arachnoiditis resulting from war injuries to the spine, and Elkington [9] reported nine instances, in six of which trauma was the sole cause. As pointed out by Paulian, Fortunescu and Tudor,[30] fracture of the vertebrae is not necessary in the production of post-traumatic arachnoid adhesions. In many cases mere concussion of the spine suffices. The third type of arachnoiditis is that secondary to other pathologic changes in the cord or spine. Arachnoid adhesions are commonly seen in the neighborhood of tumors of the spinal cord or meninges. Spondylitis is said to be one cause of secondary arachnoiditis.[11] In recent years French investigators have emphasized arachnoid adhesions arising as a reaction to various diseases of the spinal cord, such as multiple sclerosis,[31] syringomyelia [32] and Friedreich's ataxia.[33] In view of the changes in the cord in cases of severe arachnoiditis, this theory must be doubted and the possibility kept in mind that the arachnoiditis may be the primary factor and the cord changes secondary.

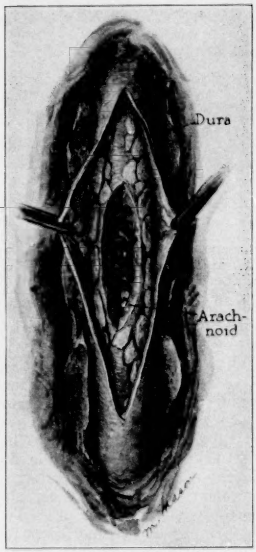

Fig. 5 (case 2).—Operative appearance. The thickened arachnoid contained gelatinous substance and was very vascular. The spinal cord was almost invisible beneath tortuous vessels. Plaques of calcium on arachnoid.

Clinical Features.—Clinically, chronic spinal arachnoiditis closely resembles extramedullary tumor of the spinal cord, especially when the arachnoiditis is limited to the formation of a single arachnoid cyst. The two conditions have in common radicular pain, slowly progressive weakness and spasticity of the extremities, impaired sensibility, exaggeration of tendon reflexes, pathologic plantar responses, and impairment of sphincteric function. In addition, the spinal fluid formula is often the same for the two conditions, consisting essentially of Froin's syndrome with a block on Queckenstedt's maneuver. Because of these striking similarities, chronic arachnoiditis is often mistaken for tumor until operation. However, an analysis of the cases here presented reveals certain differential characteristics.

In the first place, if the chronic phase follows immediately after acute meningitis, there can be little chance of a mistaken diagnosis. If the onset of the chronic phase is delayed for years after the acute disease, or if no history can be obtained of an acute stage, differentiation can often be based on the evidences of diffuse involvement of the spinal cord and roots in arachnoiditis. The pains and paresthesias in spinal arachnoiditis are widespread rather than focal and change in character and location from time to time. This feature was noted in cases 1, 3, 4 and 5 and less definitely in case 2. Sometimes the pain is poorly localized by the patient, who speaks of it as deep, aching or diffuse. Again, the superficial sensory disturbances found at examination are often vague, bizarre or inconstant in distribution and may be absent. Only in case 2 was there a marked sensory loss with a sharp level such as one expects to find with spinal cord tumor. Deep sensibility, on the other hand, and especially vibration sense, was markedly reduced or absent in the lower extremities in all but one case.

The paraplegia due to chronic adhesive arachnoiditis is not always of the spastic type, having been flaccid in cases 1 and 2 of this group. Atrophy appeared late in all five cases and was not located in a single myotome but was scattered and irregular, indicating widespread involvement of the lower motor fibers. Fibrillary twitches were not seen, but large fascicular contractions were noted in a few instances. Not infrequently, painful gross muscle spasms were a troublesome symptom, occurring in cases 1, 4 and 5. Tendon reflexes were not uniformly exaggerated, as they usually are in cases of spinal cord tumor, but were often inconsistent, some being reduced and others increased in the same case. This reduction of some of the deep reflexes, like the scattered muscular atrophy, suggests the involvement of some of the lower motor fibers as they pass the meninges.

Spinal fluid block, a sign nearly always present in paraplegia due to extramedullary cord tumor, is sometimes not found in cases of chronic adhesive arachnoiditis. No such block was found in cases 4 and 5 of this group, viz. those in which there had been no acute meningitic onset. When there is no block, the total protein content of the spinal fluid is not increased. Finally, when an injection of iodized oil is made, roentgenograms of the spine may reveal an arrest of the oil at multiple levels, as in two cases in this series.

Pathology.—The two cases studied pathologically illustrate two etiologically different types of chronic adhesive spinal arachnoiditis. The pathologic charac-

28. Barker, Lewellys, F., and Ford, Frank R.: Chronic Arachnoiditis Obliterating the Spinal Subarachnoid Space, J. A. M. A. **109**: 785-786 (Sept. 4) 1937.

29. Biemond, A.: Ueber die Meningo-radiculo-neuritis (Guillain-Barré) und die Meningo-myelo-encephalitis, betrachtet als Krankheiten bei denen das Agens primär im Meningealraum angreift, Deutsche Ztschr. f. Nervenh. **143**: 172-198, 1937.

30. Krause, Fedor: Zur Kenntnis der Meningitis serosa spinalis, Berl. klin. Wchnschr. **43**: 827-832 (June 18) 1906. Bliss, M. A.: Cysts Within the Spinal Canal, J. A. M. A. **52**: 885-886 (March 13) 1909. Sahlgren, Ernst: Ein Fall von Rückenmarkskompression durch circumscripte serose Meningitis, Zentralbl. f. d. ges. Neurol. u. Psychiat. **31**: 369, 1922. Pette,[15] Brouwer,[17] case 7. Kikuchi,[24] Paulian, D.; Fortunescu, C., and Tudor, M.: Les suites immédiates et tardives des traumatismes vertébraux: l'arachnoidite post-traumatique, Bull. d. Soc. de psychiat. de Bucarest. **1**: 76-77, 1936. Yasuda,[19] Munro.[4]

31. Alajouanine, T.; Hornet, T., and André, R.: Le feutrage arachnoidien postérieur dans la sclérose en plaques et quelques infections du névraxe, Rev. neurol. **64**: 903-911 (Dec.) 1935.

32. Alajouanine, T.; Hornet, T.; Thurel, R., and André, R.: Le feutrage arachnoidien postérieur dans la syringomyélie (sa place dans la pathologie des leptoméninges), Rev. neurol. **64**: 91-98 (July) 1935.

33. Alajouanine, T.; Hornet, T., and André, R.: Le feutrage arachnoidien postérieur dans la maladie de Friedreich et l'hérédo-ataxie cerebelleuse, Rev. neurol. **65**: 816-818 (April) 1936.

teristics, however, were almost identical in the two cases, both in the meninges and in the spinal cord itself. The tissue reactions therefore seem more or less stereotyped, regardless of differences in cause.

The meningeal changes in both cases consisted of chronic inflammation, with some mononuclear infiltration but chiefly with marked fibrosis, thickening and extensive vascularization of the pia-arachnoid. The walls of the new vessels in the sclerotic arachnoid had undergone progressive thickening, both of the adventitia and of the intima, many eventually becoming occluded. The meshes of the arachnoid were cystic and lined with arachnoid epithelium. Many roots of the spinal cord passing through these sclerotic meninges had degenerated.

The most important lesions, however, were those in the spinal cord itself, and these were unquestionably due to vascular occlusion. Such occlusive vascular changes in the spinal meninges as were seen in these cases must reduce the blood supply to the cord through the small penetrating vessels which supply the outer portions of the white matter. Thus arises the rand-degeneration reported previously and present in my two cases. This subpial degeneration was not a diffuse process in these cases but was made up of discrete and confluent focal areas of degeneration produced by the occlusion of varying numbers of the penetrating arteries. This tendency to vascular occlusion also affected the anterior spinal artery and its anterior fissural branches to the gray matter and central portions of the cord.

The exact neuropathologic characteristics of such areas of degeneration, whether in gray matter or white, seem to depend largely on the suddenness of vascular occlusion. All such regions are undergoing what is essentially anemic necrosis, but gradual, chronic occlusion apparently leads to parenchymatous degeneration, with secondary gliosis. In the white matter this process leads to a form of status spongiosus and rich proliferation of glia; in the gray matter, slow anemic necrosis leads to a degeneration of the ganglion cells, with some gliosis, but not to neuronophagia. Sudden vascular occlusion leads to rapid softening, with death of glial as well as parenchymatous tissues, and massive production of fat and little or no reaction—an anemic infarct, in short. These ischemic areas of degeneration in the cord, whether of sudden or gradual occurrence, constitute a disseminated type of focal destruction which may superficially resemble multiple sclerosis but which differs pathologically in its tendency to involve gray and white matter indiscriminately and, when acute, in the relative absence of gliosis.

Inflammatory changes were strikingly absent in the spinal cord in both case 1 and case 4. There was in no sense a myelitis, and the infection appeared to be restricted to the meninges. Neither were the changes attributable to mechanical injury to a cord fixed by adhesions in a mobile spine, as Stookey suggested.[7] Cavitation in the central regions of the cord in chronic arachnoiditis has been recorded by other workers.[34] It is a condition easily mistaken pathologically for syringomyelia (primary ependymal gliosis and cavitation). The theory that syringomyelia is primarily a degenerative disease may have been based erroneously on the observation of such cavitation.[35] In any event, cavitation of the cord may occur as a result of chronic arachnoiditis, and future studies on "syringomyelia" must take this into account.

Therapy.—In view of the pathologic conditions present, the treatment of chronic arachnoiditis is necessarily difficult. The only rational therapy would seem to be an attempt to break up the adhesions, evacuate cystic collections of fluid and remove the subarachnoid block if possible. But the arachnoid adhesions are often so widespread and vascular that surgical attack is almost impossible. Furthermore, the blood supply to the cord, tangled in the thickened pia-arachnoid, is apt to be impaired by dissection. Operation was performed in all five of my cases. Two patients died, two were unimproved and only one was clinically benefited. With the last, the operation was performed early, before the changes were marked. The advantages of surgical intervention are thus limited. Nevertheless, many good results have been reported from operation,[36] which would seem most valuable in early stages and when there are only localized arachnoid cysts. With more advanced lesions the surgeon should restrict his efforts to evacuating cysts and attempting to relieve subarachnoid block without disturbing the blood vessels.

Fig. 6 (case 4).—Fibrotic thickening and infiltration of arachnoid; partial demyelinization of spinal roots and of subpial white matter; slight secondary degeneration in dorsal columns and focal softening in dorsal horn and lateral column. Weigert-Pal and van Gieson stain; reduced from a photomicrograph with a magnification of 7 diameters.

Efforts to clear out widespread, dense or vascular adhesions will result in serious operative hemorrhage or extensive infarction in the cord.

Medical treatment should include specific measures when the cause is syphilis. Roentgen therapy, recommended by Selinsky and Harris,[37] has a doubtful rationale but may be tried.

SUMMARY AND CONCLUSIONS

In three of the five cases of chronic adhesive spinal arachnoiditis reported the condition was secondary to acute meningitis, and in the others it apparently arose spontaneously. Autopsy was carried out in two cases.

Clinically, such cases differ from those of extramedullary tumor of the spinal cord in the evidences of a diffuse disturbance of the spinal cord and roots, such as widely scattered paresthesias and pains, irregular and inconstant sensory disturbances, muscular atrophy and large fascicular twitches, painful muscular spasms, a mixture of exaggerated and diminished tendon reflexes and arrest of iodized oil at multiple levels. Spinal subarachnoid block may be absent.

Pathologically there are chronic adhesive or cystic fibrosis and vascularization of the spinal leptomeninges, with injury to the roots and secondary degeneration of

34. Schwarz,[3] Pette,[32] Harbitz and Lossius,[10] Yasuda.[39]
35. Hassin, G. B.: Histopathology of the Peripheral and Central Nervous Systems, Baltimore, William Wood & Co., 1933, p. 126.

36. Metzger,[31] Batten,[24] Schaeffer and de Martel,[34] Urechia and Jacobovici,[37] Kikuchi.[24]
37. Selinsky, Herman, and Harris, William: Radiotherapy in Disseminated Spinal Arachnoiditis, New York State J. Med. **34**: 85-87 (Feb. 1) 1934.

the dorsal columns. Thickening and occlusion of the blood vessels occur in both the meninges and the cord, with marginal degeneration of the white matter nearest the pia, and focal areas of softening in the cord, which may lead to cavitation.

Surgical intervention is of value in early stages, with only localized arachnoid cysts, but may be harmful in advanced stages with diffuse adhesions.

ABSTRACT OF DISCUSSION

DR. JOHN B. DOYLE, Los Angeles: Dr. Mackay has made a valuable contribution to the subject of chronic adhesive spinal arachnoiditis. There has been a dearth of reports of careful studies at necropsy, by which it will be possible to reach an understanding of the pathogenesis of this condition and the mechanisms of production of symptoms and to establish a sound basis for prognosis. This presentation serves to dispel certain assumptions that have crept into the literature and to provide a more inclusive clinical picture of this entity. Dr. Mackay has shown that the clinical course may be a matter of a few weeks or of several years. When the damage to the vascular supply of the spinal cord involves not only the subpial vessels but the anterior spinal artery, one may encounter paraplegia, profound sensory changes and disturbance of the vesical and anal sphincters. In certain instances many of the symptoms and signs are attributable to direct damage to the posterior spinal nerve roots. When complete spinal subarachnoid block obtains, Froin's syndrome may be present. There may or may not be associated pleocytosis. Dr. Mackay has emphasized the importance of trauma in a restricted group of cases. Keschner, Davison and Selinsky described an unusual case in which the picture developed after laminectomy for removal of a tumor of the spinal cord. In the majority of instances, however, the essential etiologic factor appears to be purulent or nonpurulent infection of the meninges. Frequently the initial meningeal process seems to have been subclinical or asymptomatic. Obviously the prognosis must be poor when there is evidence of extensive damage to the spinal cord or cauda equina. The severity and the extent of the process may be so great as to preclude successful surgical intervention.

DR. J. M. NIELSEN, Los Angeles: Dr. Mackay has made an important contribution. Frequently one observes an irregular picture of subacute combined degeneration or atypical amyotrophic lateral sclerosis and is not satisfied with the diagnosis. In 1924 I saw a patient who had been ill for a year with what was diagnosed as epidemic encephalitis. He came from the Philippine Islands. When I saw him he had symptoms referable to the spinal cord, with evidence of block, sphincteric disturbance and weakness of the lower extremities. I did a spinal puncture between the fifth lumbar and the first sacral vertebra and got 2 or 3 cc. of spinal fluid. Then I went up one space and got 2 or 3 cc. again and moved up one more space and got the same amount; I never could get any free flow; there was a complete block. I felt that nothing could be done. Then I saw a man who had spinal meningitis or leptomeningitis following skull fracture, and spinal punctures showed a thick, purulent fluid due to Bacillus mucosus capsulatus. With spinal drainage and application of mercurochrome, which was in vogue at that time, he was cured. Six years later I was called into court to testify in the case. The patient had recovered and had been back at work all those years, but he had been jarred slightly in a street car in Los Angeles. He was suing the street car company because he found that his spine was stiff and his neck a little rigid, and he could not move his lower extremities easily.

DR. R. P. MACKAY, Chicago: I will add only that chronic adhesive spinal arachnoiditis should be kept in mind in cases of so-called paraplegic multiple sclerosis. In such cases, without real evidences of disseminated lesions the diagnosis has always struck me as doubtful. I am convinced that multiple sclerosis is frequently diagnosed clinically on inadequate grounds, and in a certain proportion of these cases arachnoiditis may play a role.

EXTRARECTAL METASTATIC GROWTHS FROM UPPER ABDOMINAL AND MAMMARY CANCER

REPORT OF SEVENTEEN CASES

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The relative frequency with which extrarectal metastatic deposits are encountered, the realization that the condition is seldom recognized and the fact that the condition has been confused with and incorrectly diagnosed as primary rectal carcinoma prompt a brief discussion of this entity, since it invades many fields of scientific medicine.

Seventeen cases that have come under my observation during a comparatively short period are reported here.

CASE 1.—J. W., a Negro aged 49, admitted to the hospital April 3, 1937, because of abdominal pain, had been in good health until the previous January, when pain was experienced in the pit of his stomach immediately after eating. During the past two weeks difficulty, as well as frequency, and a burning sensation on urination had been noted. Bowel movements had been associated with straining for the past month; the stools had been tarry for several weeks. The patient said that he had lost 15 pounds (6.8 Kg.) in three weeks. The family history was irrelevant. On physical examination a mass the size of a walnut was palpated in the right upper quadrant at the edge of the rectus. By rectum a large irregular mass was felt anterior to the wall, which was thought to be a malignant growth on the prostate. The urine was yellow and alkaline; the specific gravity was 1.022; there was no albumin or sugar, and occasional epithelial cells were seen. A blood count showed 4,040,000 erythrocytes, 78 per cent (12 Gm.) of hemoglobin and 13,700 leukocytes, with 64 per cent polymorphonuclears, 25 per cent lymphocytes, 4 per cent monocytes, 6 per cent eosinophils and 1 per cent basophils. The Wassermann and Kahn tests of the blood were negative. Chemical analysis of the blood showed 82 mg. of sugar, 11 mg. of urea, 118 mg. of cholesterol and 78 mg. (66 per cent) of cholesterol esters per hundred cubic centimeters. The icterus index was 7. The total protein content was 6.62 mg. per hundred cubic centimeters, the albumin making up 4.19 mg. and the globulin 2.43 mg. The feces showed no parasites or ova. Gastric analysis showed no free hydrochloric acid, 12 units of total acid, a trace of occult blood and no starch. Cystoscopic examination April 6 disclosed no residual urine, moderate generalized cystitis, distortion of the vesical neck and no evidence of intravesical malignant growth. X-ray examination April 20 showed the stomach normal in outline, size and position, marked evidence of hyperperistalsis and hypermotility and no defects along the walls or curvatures. A normal duodenal cap was outlined. There was no six hour gastric retention; barium sulfate was present from the terminal portion of the ileum to the middle of the descending colon. An opaque enema showed no pathologic lesion of the rectum or large intestine. X-ray examination April 26 revealed no evidence of metastases to the lumbar vertebrae or the bones of the pelvis. No biliary calculi could be demonstrated on the flat film. The liver was seen but was not enlarged. In cholecystograms made April 29 the gallbladder showed no function. No calculi could be demonstrated. A flat plate of the right kidney and a retrograde pyelogram May 9 showed that both kidneys were apparently functioning, though at no time was much dye evident. The dye was seen better in the right kidney, and there was no evidence of hydronephrosis. The flat film showed no evidence of calculi. Neither kidney was mobile.

With the provisional diagnosis of primary malignant growth of the gallbladder or prostate and partial intestinal obstruction, the patient was transferred to the radiologic department.

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Read before the Section on Gastro-Enterology and Proctology at the Fifty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

Examination of the rectum showed it to be almost completely obstructed by a large extrinsic horseshoe-like mass on the anterior and both lateral aspects. The process was hard, nodular, asymmetric and distinctly outside the rectal wall. The mucous membrane was movable. Between the lower edge of the extrarectal mass and the smooth dome of the prostate a horizontal crevice could be noted by the examining finger.

May 28 an exploratory laparotomy was performed, which showed carcinoma of the head of the pancreas, with metastasis to the parietal peritoneum, omentum and mesosigmoid. The rectovesical pouch was literally filled by a large nodular growth. The patient died, but autopsy was not permitted.

CASE 2.—F. D., a white man aged 60, admitted to the hospital Aug. 2, 1937, because of "bowel trouble," stated that he had been fairly constipated for the past year and during the past four months had been compelled to take increasing amounts of various laxatives. The stools were watery. The abdomen appeared normal, but rectal examination August 3 revealed a large, hard nodular mass located in Blumer's shelf. There was no palpable or visible evidence of an intrinsic process. The diagnosis was extramural malignant growth from some upper intestinal site. X-ray examination August 7 disclosed a large filling defect at the pars media of the stomach, extending to the pyloric end. The irregularity and defect were seen fluoroscopically and on all films. There was no six hour gastric retention. The diagnosis was malignant growth of the stomach. This patient was discharged after receiving high voltage roentgen therapy and died at his home one month later.

CASE 3.—J. L., a white man aged 48, admitted to the hospital Oct. 9, 1936, because of pain in the right costal region and loss of weight, had been well until the previous April, when he noticed a sharp pain under the ribs on the right side. This had been more or less constant but worse at night. There was no relation between the pain and eating. He had been constipated for many years; there had been no tarry stools. He had lost 27 pounds (12.2 Kg.) in six months. Physical examination of the abdomen gave negative results; by rectum a stony-hard fixed mass, approximately the size of a large orange anterior to and encroaching on the rectal wall was palpated. The lumen of the rectum was almost entirely occluded. An exploratory laparotomy November 4 showed generalized carcinomatosis, the omentum being infiltrated with small mucoid nodular growths. Biopsy showed carcinoma, mucoid variety, secondary in the omentum. The patient was discharged but returned to the radiologic service, where high voltage roentgen therapy was given. Necropsy March 5, 1937, disclosed primary adenocarcinoma of the ascending colon type 3, mucoid variety, secondary carcinoma of the lymph nodes and a large metastatic deposit in the rectovesical pouch, causing partial obstruction.

CASE 4.—N. F., a white man aged 55, admitted Oct. 28, 1937, because of intermittent constipation and diarrhea and pain in the lower part of the abdomen, stated that for four months he was compelled to take laxatives and enemas, after which the diarrhea became a more or less prominent feature. The abdomen was found to be tense, with dulness in the flank. By rectum a firm constriction, which would not permit passage of the finger, was felt approximately 2 inches above the anorectal line. The process was more marked on the anterior wall; the mucous membrane was nonulcerated and movable over the mass. The diagnosis of primary carcinoma of the rectum was made. Biopsy showed chronic inflammatory tissue, so that another diagnosis was made of primary carcinoma of the prostate. Cystoscopic examination showed no evidence of a malignant process. X-ray examination October 29 disclosed an abnormal contour of the rectum; an opaque enema showed no other evidence of a pathologic lesion. Exploratory laparotomy was performed December 20, at which time carcinoma of the ascending colon with widespread intra-abdominal metastases was found. Biopsy showed adenocarcinoma secondary in the mesentery; an extensive collar-like nodular mass was found impinging on and completely encircling the rectum. The patient died December 22; autopsy was not permitted.

CASE 5.—J. O'H., a white man aged 70, admitted to the hospital March 3, 1936, because of pain in the stomach, stated that the pain was dull and continuous but worse after meals and radiated to the right arm. There was no vomiting. He had lost 10 pounds (4.5 Kg.) in six weeks. In the past history "stomach trouble" for thirty years was cited. Physical examination gave negative results except to reveal a firm irregular mass the size of an egg, 4 cm. above the anal margin. The patient was transferred to the radiologic department, with the provisional diagnosis of carcinoma of the rectum. Examination of the rectum March 5, 1938, showed a fixed nodular growth anterior to the rectal wall. The mucosa was freely movable and devoid of ulcerative change. There was extrarectal metastatic malignant growth. The patient was too weak to be studied. Necropsy March 15 showed adenocarcinoma type 3 of the head of the pancreas, with multiple intra-abdominal metastases, especially in the rectovesical pouch.

CASE 6.—D. McC., a white man aged 50, admitted to the hospital Feb. 8, 1937, because of pain in the stomach, had been in apparent good health until three weeks before, when he became conscious of pain in the right lower quadrant, not severe but constant. He had lost about 10 pounds (4.5 Kg.) in six months. Through the right anterior part of the abdominal wall a hard, fixed mass was palpable. By rectum a large nodular growth was felt anteriorly, approximately 3 inches above the anal margin. A diagnosis of primary malig-

Fig. 1 (case 7).—Metastatic lesion, showing a similar picture, with more marked stromal reaction. The cells again occur in strands and singly for the most part, rather than in any organoid arrangement.

nant tumor of the rectum was made. X-ray examination following a barium sulfate enema February 14 demonstrated a defect in the ascending colon just distal to the cecum. Reexamination March 8 confirmed the presence of a filling defect. An exploratory operation was done March 15, at which time an extensive carcinoma of the ascending colon was found. A nodular mass was palpated in the rectovesical pouch. Biopsy of the parietal peritoneum and omentum showed adenocarcinoma type 4 of the colon. The patient died March 30, but autopsy was not permitted.

CASE 7.—A. G., a white man aged 39, admitted to the hospital Sept. 22, 1937, because of abdominal pain and difficulty in swallowing, had been apparently well until May 1937, when he noticed a dull, gnawing pain in the right upper quadrant of the abdomen, which occurred immediately after eating. X-ray examination by Dr. Holmes October 20 showed marked contracture of the entire stomach. Fluoroscopically there was so much contraction of the pars media and the pyloric end of the stomach as to permit little barium sulfate to pass through into the duodenum.

As evidenced by rectal examination, two hard masses approximately the size of a small walnut were palpable anterior to and outside the rectal wall. The mucosa was freely movable over the metastatic deposits. The abdomen was explored October 27 during nitrous oxide anesthesia, and an extensive

carcinoma of the stomach with evidence of widespread metastasis and nodules in the rectovesical pouch was seen. Biopsy of the stomach showed adenocarcinoma grade 4; the growth in the culdesac showed metastatic carcinoma. The patient died March 13, 1938. Autopsy showed scirrhous adenocarcinoma of the stomach. The right pelvic wall presented firm white lumps which surrounded the ureter and compressed it just proximal to the bladder. White pinpoint nodules were scattered along the pelvic wall in front and at the sides of the rectum.

CASE 8.—M. C., a Negress aged 58, admitted to the hospital in April 1938 because of abdominal pain, being extremely ill had difficulty in relating past events, but a relative stated that severe abdominal pain radiating to the back had been experienced for two months. No nausea or vomiting was present; the loss of weight was considerable, with progressive constipation. Examination showed the liver to be somewhat enlarged and the abdomen distended. Chemical analysis of the blood showed 112 mg. of sugar, 70 mg. of urea, 19 mg. of phosphatase, 8.5 mg. of calcium, 3.7 mg. of phosphorus, 416 mg. of cholesterol and 74 mg. of cholesterol esters per hundred cubic centimeters. The icterus index was 218. The blood count showed

Fig. 2 (case 10).—Retroperitoneal fibrosarcoma made up of interlacing bundles of young fibroblasts, showing considerable pleomorphism, anaplasia and a moderate number of mitotic figures. The tumor is highly vascular. Metastatic lesion, showing similar structure but with evidence of greater malignancy. The cells are more irregular in size and shape; the nuclei are much more hyperchromatic. There is considerable necrosis.

5,440,000 erythrocytes, 91 per cent (14 Gm.) of hemoglobin and a differential count of 72 per cent polymorphonuclears, 24 per cent lymphocytes and 4 per cent small lymphocytes. Autopsy May 8 disclosed primary carcinoma of the common bile duct, with generalized carcinomatosis. There were numerous metastatic nodules in the culdesac.

CASE 9.—W. C., a Negro aged 67, was admitted to the hospital April 28, 1937, complaining of soreness about the umbilicus. This had begun three months before, after he had lifted a concrete block; since that time he had experienced frequent attacks of pain radiating through the abdomen. Weakness and loss of weight (60 pounds [27.2 Kg.]) in six months were cited. The abdominal wall below the umbilicus was tender to the touch and small hard nodules were palpable beneath the skin. By rectum a slightly movable nodular mass, approximately the size of a tangerine, was found anterior to and encroaching on the rectal wall. The mucosa was freely movable over the growth and not ulcerated. The diagnosis was extrarectal metastatic malignant growth. Necropsy June 4 showed primary adenocarcinoma of the stomach type 3 and secondary carcinoma of the liver, gallbladder, spleen, pancreas, umbilicus and intra-abdominal lymph nodes. The rectovesical pouch was the site of a few small implants and one large growth approximately the size of an orange.

CASE 10.—E. S., a Negress aged 53, admitted to the hospital June 21, 1937, with a mass in the abdomen, could not furnish a history because of an apparent toxic psychosis. Examination revealed a large mass involving the entire upper part of the abdomen; it was firm, nontender and immovable. Immediately above the pubis a hard subcutaneous nodule about the size of a walnut was palpated. By rectum a large hard nodular mass was felt anterior to the wall. X-ray examination June 1 disclosed that in the supine position the stomach was elongated and barium sulfate incompletely filled the stomach, owing to extrinsic pressure along the lesser curvature. The mucosal rugae in the pars media were clearly visualized, and the pylorus appeared to be flattened as a result of the enlarged liver. Autopsy July 5 disclosed retroperitoneal tumor and neurogenic sarcoma with involvement of the heart, lungs, liver, adrenals and retroperitoneal lymph nodes. Beneath the peritoneum and anterior to the rectum a large metastatic process was found.

CASE 11.—W. H., a white man aged 62, admitted to the hospital Jan. 31, 1938, because of pain in the stomach, stated that he had been well until ten weeks before, when there developed pain in the epigastrium after meals and gaseous distention. Physical examination showed some rigidity in the upper midepigastric region. Gastric analysis showed no free hydrochloric acid, 30 units of total hydrochloric acid and some occult blood. Gastrointestinal study revealed that the stomach was small, contracted and somewhat fixed. Rectal examination showed three palpable nodular masses in the rectovesical pouch. All were immovable and hard. An exploratory laparotomy February 21 showed an extensive carcinoma of the stomach with generalized visceral and parietal peritoneal metastases. A nodule removed at operation was reported to show adenocarcinoma of the stomach, secondary in the peritoneum. At autopsy February 22 primary scirrhous carcinoma of the stomach was seen, with implantation carcinoma of the intestine and peritoneum. The abdominal lymph nodes showed metastatic carcinoma and numerous implantations of carcinoma in the region of the sigmoid flexure and in the rectovesical pouch.

CASE 12.—H. G., a white woman aged 37, admitted Jan. 5, 1934, to the Philadelphia General Hospital because of swelling in the breast, stated that in April 1933 she had noticed three small lumps in the left breast. She had been operated on at another hospital after three months, during which period the lumps had become egg sized; only the masses were removed. The following September nodules developed throughout the left breast and axilla. Roentgen therapy was then administered. She now complained of pain in the left shoulder and lumbar region, as well as shortness of breath. Physical examination showed an oblique scar representing left radical mastectomy, numerous small glands in the left supraclavicular region and a tumor mass occupying the entire right breast, with large glands in the right axilla. X-ray examination January 16 by Dr. H. W. Ostrum showed metastatic carcinoma of the lungs. Autopsy March 3 showed adenocarcinoma type 4, secondary carcinoma in the lungs and shaggy masses in Douglas' pouch. Nodules varying in size from that of a pea to that of a pinhead were scattered all over the peritoneum. In Douglas' pouch they were confluent.

CASE 13.—A. B., a white man aged 43, admitted to the hospital Dec. 15, 1936, because of pain in the stomach, described the pain as dull, worse after meals and associated with some vomiting. He had passed tarry stools mixed with some bright red blood for eight months. The report from another hospital showed that he had been operated on one year previously for gastric ulcer. There was a questionable mass in the upper right quadrant of the abdomen and a circumferential extrinsic narrowing of the rectum. The mucosa was nonulcerated and movable over the mass. Gastrointestinal study by Dr. H. W. Ostrum December 18 with the patient erect showed a large filling defect of the lesser curvature involving a greater portion of the pars media and pars pylorica. There were moderate deformity of the pyloric end of the stomach and flattening of the duodenum, especially of the first portion. In two hours there was approximately 30 per cent retention. The diagnosis

was carcinoma of the lesser curvature involving the pars media and pars pylorica. Punch biopsy of material taken from the extrarectal growth through the rectum showed metastatic adenocarcinoma. Extensive high voltage roentgen therapy was given. To my knowledge the patient is still living, in another state.

CASE 14.—M. St. P., a white woman aged 47, admitted to the hospital April 19, 1937, complaining of pain in the abdomen, stated that she had felt a mass in the abdomen the previous December and that she vomited after eating any type of solid food. The remainder of the history was irrelevant. Physical examination showed an emaciated woman with a hard nodule in the left supraclavicular fossa and a definite hard nodular mass in the left side of the hypochondrium, extending along and under the costal margin. The latter nodule, approximately the size of a lemon, was movable. By rectum a large hard nodular growth anterior to and outside the wall of the rectum was palpated. The mucosa was freely movable. X-ray examination April 14 disclosed marked narrowing and fixation of the cardiac end of the stomach and pars media. There was irregularity along the lesser curvature. Autopsy showed primary adenocarcinoma of the stomach with widespread metastasis. A large metastatic deposit was seen in the recto-uterine pouch.

CASE 15.—J. C., a white man aged 47, admitted to the hospital Dec. 3, 1937, because of pain in the epigastrium, stated that he had been well until two months before, when he noticed pain in the shoulder and in the ribs. The patient was given medication, but he said that it seemed to aggravate the discomfort. Finally he was unable to eat because of the pain; there was no nausea or vomiting. He had been markedly constipated during this period and had lost considerable weight. The lower edge of the liver was palpable. A mass the size of a fist was felt in the upper quadrant, slightly to the right of the midline. There was considerable ascitic fluid. By rectum a large smooth fist-sized mass was palpable anterior to the rectum and encroaching on it. The mucous membrane was freely movable. Autopsy showed primary type 4 adenocarcinoma of the stomach with generalized carcinomatosis. The rectovesical pouch was readily filled with numerous small and one large metastatic growth.

CASE 16.—C. F., a white woman aged 63, admitted to the hospital Jan. 24, 1937, because of pain in the head, had noticed a lump in the left breast for which she was treated with ultraviolet rays early in 1936. In the spring of the same year she noticed stiffness of the neck and pain in the head, arms and legs. She had lost considerable weight. An increase in constipation was experienced. Examination showed the left breast to be hard and fixed, with definite retraction of the nipple. There was no axillary or supraclavicular adenopathy. X-ray examination January 24 disclosed extensive carcinomatous metastasis to the skull, jawbones and cervical and dorsal vertebrae. Some of the ribs were involved. There was possible involvement of the acromion process. Extensive high voltage roentgen therapy was given. She returned to the radiologic clinic April 21, 1938. At this time she complained of pain in the abdomen, pain at defecation and increasing constipation. Multiple hard nodules were felt through the anterior part of the abdominal wall. By rectum a hard irregular collar-like mass partially encircling the anterior portion was palpable. The mucous membrane was movable over the extrinsic constriction. The patient is still living.

CASE 17.—C. O., a white man aged 55, was admitted to the hospital in January 1938 because of intermittent pain in the right lower quadrant of eight months' duration, dyspnea and loss of 15 pounds (6.8 Kg.). Examination disclosed a hard fixed mass in the right upper abdominal quadrant, ascites and, by rectum, a hard nodular constricting process extrinsic to the wall. Autopsy May 22 revealed primary adenocarcinoma of the right kidney with generalized carcinomatosis and a rectovesical pouch obliterated by metastatic deposits encroaching on and constricting the rectum.

In the presentation of such a subject as this certain phases warrant some discussion: What is the historical background of this peculiar phenomenon? What is understood by the "rectal shelf"? What is its significance? Where is the usual site of the primary growth? What is the mode of spread? From what is it to be distinguished? What is its prognostic value, and, finally, what form of treatment can be prescribed?

The earliest reference I have found is that by Strauss,[1] who some forty odd years ago reported a case of gastric carcinoma with metastasis to the pouch of Douglas. Four years later this investigator [2] cited two additional cases and mentioned that such metastasis not only may be early but may be the only manifestation. Schnitzler [3] in 1908 reported eleven cases, in one of which the pancreas and in all others the stomach was the primary site. Worthy of mention is this quotation from the original German: "The important feature was that all these patients consulted the doctor for symptoms produced by the metastasis, without having the slightest suspicion of the presence of the

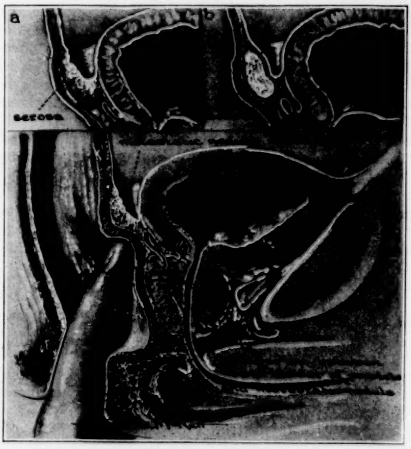

Fig. 3.—Sagittal section, showing the tip of the finger between the prostate and a growth on the culdesac; *a*, supraserosal mass and, *b*, subserosal mass.

primary growth." In his report Schnitzler mentioned that in one case he mistook the tumor for a primary rectal growth and performed a radical sacral extirpation. Further examination of the patient, who survived six months, revealed a gastric carcinoma of long latency. Payr [4] described a case in which he performed a colostomy for rectal stenosis due to periproctitic and parametritic induration. The patient died of peritonitis; autopsy revealed a gastric carcinoma and the presence of perirectal metastasis of the infiltrative type. Additional cases were reported by Toyosumi,[5] Chiari,[6]

1. Strauss, Hermann: Ueber die Abhängigkeit der Milchsauregährung Von. HCl-Gehalt des Magensaftes, Ztschr. f. klin. Med. **28:** 584, 1895.
2. Strauss, Hermann: Nebst Bemerkungen über die Bedeutung des Befundes von Eiter and Blut im Magen sowie gewisser wenig beobachteter Krebs-Metastasen die Diagnose des Magencarcinoms, Berl. klin. Wchnschr. **36:** 872, 1899.
3. Schnitzler, J.: Ueber eine typische lokalisierte Metastase des Magencarcinoma, Med. u. Chir. **19:** 205, 1908.
4. Payr, E.: Ueber gleichzeitige Stenosirung von Pylorus und Darm, Arch. f. klin. Chir. **75:** 291, 1904-1905.
5. Toyosumi, H.: Ein Fall von Stenose des Rectum durch metastatischen Karzinom bei gleichzeitigen metastasierendem Myelom, Virchows Arch. f. path. Anat. **191:** 70, 1908.
6. Chiari, H.: Zur Kenntnis der hämatogenen Geschwülstmetastasen im weiblichen Genitalapparate, Prag. med. Wchnschr. **30:** 17 (April) 1905.

Orth,[7] Kappeler,[8] Kelling,[9] Kaufmann,[10] Brosch[11] and Bensaude and Okenczyc.[12] Blumer[13] in 1909 reviewed the literature at hand in addition to reporting two cases; in one the primary site was the gallbladder and in the other the stomach. By virtue of his excellent description this extrarectal site has been referred to frequently as Blumer's shelf. Since that time few reports have been published,[14] although several quotations or reviews are to be found.[15]

Metastatic deposits in the culdesac under ordinary circumstances can be palpated through the anterior or anterolateral wall of the rectum according to their anatomic distribution. Growths the size of a pea may be felt occasionally, although it has been my experience that the size estimated by digital examination of the rectum is not always verified by operation or necropsy. Coalescence of these deposits, which vary in shape, size and number, produces a ledge spoken of as the rectal shelf.[1] In such a case digital examination of the rectum elicits a nodule or growth anterior or anterolateral to the rectal wall approximately 2 to 4 inches above the anal margin in the female or one-half inch above the prostate in the male. As would be expected, it is hard and not tender. Ordinarily a sulcus can be felt between the upper rounded border of the prostate and the mass. The mucosa of the rectum, being uninvolved, is freely movable over the growth; this, it should be remembered, is the main feature distinguishing it from primary carcinoma of the rectum. Increase in size and extent may readily cause impingement on the anterior rectal wall, in which case the examining finger encounters backward displacement of the rectum by a mass anterior to and outside its wall. Occasionally the metastatic process encircles the rectum so as to cause occlusion, either partial, as in cases 1, 4, 13, 15, 16 and 17, or complete, as in that reported by Chiari.[6] In each case the mucosa was freely movable over the growth. Of course it is possible, as reported by Kappeler,[8] for the process to infiltrate the rectal wall proper and cause fixation of the mucous membrane, under which circumstance it would not be unlikely that the resultant proliferating changes might be confused with primary carcinoma; yet in my series of cases, even those of almost complete obstruction, the mucosa was movable and free from ulceration. This condition is significant in that patients may consult the physician because of symptoms produced by the metastasis without the slightest suspicion of an existing primary growth elsewhere. Such growths in themselves may direct attention to the primary malignant process in another site. That such metastatic deposits may cause narrowing of the rectal lumen, even to the point of complete obstruction, and that these tumors may be mistaken for primary rectal carcinoma are factors only too significant.

Judging from the available literature at hand as well as my own series of cases, the stomach is by far the most common primary site. Feldner[16] said that metastasis to Douglas' pouch occurs in 20 per cent of cases of gastric carcinoma and in 18 per cent of cases of carcinoma of the gallbladder. Such frequency I have been unable to confirm. The only cited case of involvement of the gallbladder is that of Blumer.[13] Schnitzler,[3] it will be recalled, reported involvement of the pancreas in one case and of the stomach in ten cases. Melchior[17] reported three cases; the stomach, esophagus and the breast were the sites. Both Handley[18] and Carnett[19] described three cases of carcinoma of the breast with metastasis to the culdesac. The sites in the reported cases are shown in table 2.

In referring to cancer of the breast the words of Handley[18] may be recalled: "It must never be forgotten that the first sign of epigastric invasion may be found not in the epigastric region, but in the pelvis." Eusterman and Balfour[20] have said "Although the gastrocolic and greater omentums are favorite sites, the most common situation is the pelvic peritoneum."

The question arises as to the manner in which the culdesac is invaded. While there is no conclusive proof as to the mode of spread, it seems pertinent to review briefly the opinions and investigations of various workers. By metastasis is understood the dissemination of a malignant growth either by continuous extension or by tumor cell emboli. Many writers lean toward dissemination by the hematogenic route, which, it is agreed, is the usual means of spread in the case of sarcoma (case 10). As I have previously stated,[21] it is recognized that an implantation type of cancer does exist, and several authentic cases have been reported.[22] Carcinomatous implants in the abdomen, especially in cases of advanced disease, are not uncommon. The explanation first mentioned by Schnitzler is today almost universally accepted, in that pelvic involvement from a malignant growth of the stomach or gallbladder occurs by gravitation of fragments of cancerous tissue to the pouch, for it will be recalled that he attributed the relative frequency of the disease in males and rarity in females to malignant cells' reaching the rectovesical space in the former whereas they were caught by or

7. Orth, Johannes: Compendium der pathologisch-anatomischen Diagnostik, ed. 6, Berlin, A. Hirschwald, 1900, p. 483.
8. Kappeler, Otto: Meine Erfohrungen über Magenresection wegen Carcinom, Ztschr. f. Chir. **64**: 247, 1902.
9. Kelling, G.: Zur Resection des carcinomatösen Magens, Arch. f. klin. Chir. **75**: 229, 1905.
10. Kaufmann, C.: Lehrb. der spez. path. Anat. **2**: 385, 1901.
11. Brosch, O.: Ein seltener Fall von multiplen karzinomatosen Strikturen des Darmes, Arch. f. klin. Med. **57**: 606, 1896.
12. Bensaude, R., and Okenczyc, C.: Retrécissements cancereux multiples de la partie sous-diaphragmatique du tube digestif, Arch. de méd. expér. et d'anat. path. **18**: 526, 1906.
13. Blumer, G.: The Rectal Shelf: A Neglected Rectal Sign of Value in the Diagnosis and Prognosis of Obscure Malignant and Inflammatory Disease Within the Abdomen, Albany M. Ann. **30**: 361 (May) 1909.
14. Keith, A. R.: Clinical Significance of So-Called Rectal Shelf, Tr. Am. Proc. Soc. **28**: 46, 1928, and discussion by R. W. Jackson, p. 50. Melchior.[17] Handley.[18] Carnett.[19] Carnett.[35b]
15. These include:
Babcock, W. W.: Textbook of Surgery, ed. 2, Philadelphia, W. B. Saunders Company, 1935, p. 975.
Bacon, H. E.: Metastatic Growths to Rectal Shelf: Report of Seven Cases, read before the Proctologic Society, Graduate Hospital of the University of Pennsylvania, March 1937.
Earle, S. T.: Report of Proctologic Literature, Tr. Am. Proct. Soc. 1910, p. 22.
Irsigler, F. J.: Die Röntgenuntersuchung beim Mastdarmkrebs, insbesondere beim Krebs des hohen Rektums, Beitr. z. klin. Chir. **165**: 530, 1937.
Livingston, E. M.: A Clinical Study of the Abdominal Cavity and Peritoneum, New York, Paul B. Hoeber, Inc., 1932, p. 48.
Schofield, J. D.: Verbal communication to the author, December 1937.
Yeomans, F. C., in Blumer, George: Bedside Diagnosis, Philadelphia, W. B. Saunders Company, 1929, vol. 1, pp. 798 and 836.
Yeomans, F. C.: Proctology, New York, D. Appleton-Century Company, 1936, p. 505.
Feldner.[16]
Eusterman and Balfour.[20]
16. Feldner, cited by Yeomans, F. C.: Proctology, New York, D. Appleton-Century Company, 1936, p. 505.
17. Melchior, L.: Perirectal Carcinoma, Ugesk. f. lager. **82**: 231 (Feb. 12) 1920.
18. Handley, W. S.: Cancer of the Breast, ed. 2, New York, Paul B. Hoeber, Inc., 1922, p. 234.
19. Carnett, J. B.: Scirrhous Carcinoma of Breast with Extensive Metastases, S. Clin. North America **7**: 7 (Feb.) 1927.
20. Eusterman, G. B., and Balfour, D. C.: The Stomach and Duodenum, Philadelphia, W. B. Saunders Company, 1935, p. 103.
21. Bacon, H. E.: Multiple Primary Malignancy of the Anus, Rectum and Sigmoid Colon: Report of Six Cases, read before the American Proctologic Society, San Francisco, June 1938; The Anus, Rectum and Sigmoid Colon, Philadelphia, J. B. Lippincott Company, 1938. Bacon, H. E., and Gilbert, P. D.: Sites of Metastases from Carcinoma of the Anus, Rectum and Sigmoid Colon in a Series of 318 Cases, read before the Proctologic Society, Graduate Hospital of the University of Pennsylvania, May 9, 1938.
22. Borrmann, R.: Statistik und Casuistik über 290 histologisch untersuchte Hautcarcinome, Deutsche Ztschr. f. Chir. **76**: 404, 1905. Fenger, Christian: Double Carcinoma of the Colon, J. A. M. A. **11**: 606 (Oct. 22) 1888. Hoche, L.: Du cancer gastrique secondaire, Presse méd. **1**: 67, 1901. Maingot, R.: Multiple Carcinomata of the Rectum, Tr. M. Soc. London **50**: 121, 1927.

became engrafted on the ovaries in the latter. Eusterman and Balfour [20] have said that apparently when the tumor reaches the gastric serosal layer, carcinoma cells are mechanically carried to the pelvis and there occasionally take root. This, however, while possible and highly probable, does not explain entirely the occurrence of an isolated metastatic pelvic deposit in the absence of other visible and palpable implants. In two instances sections of the smaller retroperitoneal lymphatic vessels in the lower dorsal and lumbar regions presented evidence of malignant invasion. Some investigators contend that lymphatic embolism and continuous permeation are commonly associated. Ewing [23] called it probable that the rapidly growing epidermoid and glandular carcinomas disseminate chiefly by lymphatic embolism, while the slowly growing and recurrent tumors often extend by continuous permeation. Retrograde flow through lymphatic and blood channels is a subject that always invites discussion. Organs in which there is a normal venous pulse or in which violent expiration or increase of intrathoracic pressure occurs would be the most common sites. Occlusion of the main lymphatic or venous channels gives rise to disordered function, as a result of which retrograde flow, even though a slow process may supervene. Examples of retrograde venous and lymphatic flow have been cited by Heller, Bonome, Arnold, Ernst and von Recklinghausen, Vogel, Poncet, Most and Troisier.

Cases in the Literature

Author	Primary Site	No. of Cases
Strauss (footnotes 1 and 2)	Stomach	3
Blumer [13]	Stomach	2
	Gallbladder	1
Orth [7]	Stomach	1
Kelly, H. A., and Burnam, C. F.: Diseases of the Kidneys, Ureters and Bladder, New York, D. Appleton & Co., 1922, vol. 2, p. 254	Kidney	1
Schnitzler [3]	Stomach	10
	Pancreas	1
Kelling [9]	Stomach	1
Kappeler [8]	Stomach	5
Payr [4]	Stomach	1
Chiari [6]	Stomach	1
Handley [18] (p. 140)	Breast	3
Jackson [14]	Stomach	1
Carnett [19]	Breast	3
Keith [14]	Stomach	1
Toyosumi [5]	Stomach	1
Irsigler [15]	Stomach	1
Schofield [15]	Stomach	1
Melchior [17]	Esophagus	1
	Stomach	1
	Breast	1
		41

Walther [24] believes that a large number of cases of alleged retrograde lymph node metastasis are instances of continuous dissemination, because in the majority of his cases he was able to demonstrate that diseased lymph nodes not in the vicinity of the primary growth represented regional metastases of an organ that had become involved by the hematogenic route.

Regarding carcinoma of the breast, Handley maintained that in nearly every case dissemination to the abdominal cavity occurs by transcelomic spread, the secondary deposits arising from gravitations of cancerous particles into the pelvis, and that in the late stage the whole pelvis may be filled with cancer and its contents matted together. Carnett [25] concurred in the view that lymphatic permeation is a common process in the liver and that in other parts, especially the deeper or pelvic parts of the abdomen, lymphatic permeation may begin around implanted nodules. He differed, however, in expressing the belief that widespread lymphatic permeation may occur in the abdomen in the absence of implants.

A number of conditions may simulate a metastatic growth in the culdesac, and from these it must be differentiated. Among them should be mentioned adherent coils of small intestine and omentum encountered in certain types of peritonitis, especially the diffuse tuberculous variety, scybala in the small bowel, subperitoneal myoma, carcinoma of the sigmoid flexure prolapsing into the pouch, and chronic inspissated, partially encapsulated pelvic abscess in the process of organization; carcinoma of the upper pole of the prostate or of the posterior bladder wall infiltrating the rectum, loculated pelvirectal abscess, hypertrophied valve of Houston, endometriosis of the rectovaginal septum or distal part of the sigmoid flexure and extension from an ovarian or uterine malignant growth. No difficulty should arise in distinguishing primary rectal carcinoma except in rare instances in which the metastatic process infiltrates the rectal wall.

So far as prognosis and treatment are concerned, this sequence is of utmost importance in that it represents an advanced stage of the disease for which radical surgical measures are contraindicated. A palliative procedure, however, such as some type of enterostomy, may be performed according to the individual case.

SUMMARY AND CONCLUSIONS

Of seventeen patients with extrarectal metastatic malignant growth from remote sites, twelve were men and five women, thirteen were white persons and four Negroes. The ages ranged between 37 and 70, averaging 53 years. The stomach was the most frequent site of primary growth. As to type, sixteen tumors were adenocarcinomas and one was a sarcoma. Grading of the tumor was made in eight cases; four were of grade 4 and four of grade 3. In four cases the symptoms were suggestive of disturbance of the lower bowel.

In six instances the extrarectal metastatic process was diagnosed as a primary growth of either the rectum or the prostate. In five cases there was definite constriction of the rectum. In all seventeen cases the mucosa was devoid of fixation and ulceration.

Whereas in all cases in this series the disease was advanced, it must be realized that such metastasis may occur early and be the only extension. The condition is of importance in that it is not extremely rare, the symptoms may not direct attention to the primary site and the extrarectal process may be incorrectly diagnosed.

As a routine procedure careful palpation and visualization of the rectum in every case of suspected malignant growth are advocated.

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ABSTRACT OF DISCUSSION

DR. NEWTON D. SMITH, Rochester, Minn.: On reviewing Dr. Bacon's paper one notes that many efforts have been made to explain the occurrence of the so-called rectal shelf in cases in which the primary lesion is in some distant part of the body. Yet none have been universally accepted or demonstrated. An unsolved problem has been offered. The mechanical, physiologic and pathologic aspects of this problem are worthy of further study. The element of diagnostic error in this series of cases

23. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1919, p. 77.

24. Walther, H. E.: Investigations on Cancer Metastasis, Ztschr. f. Krebsforsch. **46**: 334 (Sept. 30) 1937.

25. Carnett, J. B.: (*a*) Malignant Metastasis Other Than to the Regional Lymph Nodes, Arch. Surg. **18**: 811 (March) 1929; (*b*) Carcinoma of the Breast with Metastases to Lymph Nodes, Skin, Epicardium and Bones, S. Clin. North America (pt. 2) **7**: 283 (April) 1927.

is a severe criticism. In more than 34 per cent there was an error in the early diagnosis. This error consisted of discovering the primary lesion and overlooking the rectal shelf or, conversely, discovering the rectal shelf and, assuming it to be a primary lesion, failing to search further for the real source. The importance of an extrarectal metastatic growth as a factor in determining prognosis and treatment seems undeniable in view of the cases reported by Dr. Bacon. If this were not so evident, my second point would assume only academic importance. The seventeen cases reported reveal that the life expectancy of the patient in whom a rectal shelf is discovered on examination is usually not more than several months. Assuredly, with this evidence radical or curative surgical procedures are contraindicated and only that surgery should be attempted which is necessitated by the physician's effort to prolong life or relieve actual suffering.

DR. WILLIAM H. DANIEL, Los Angeles: These extrarectal metastases or implantations present definite problems as to diagnosis because in the majority of cases the rectal lesion is the first noticed and the symptoms from the primary lesion are so mild that they are overlooked by the patient. When the rectum is constricted by an annular or localized mass and the mucosa is not involved, and cancer of the cervix or prostate is ruled out, carcinoma in the upper part of the abdomen must be considered. Of twelve cases of this type that I have seen, eight were diagnosed as of remote origin, six of which were confirmed at operation and one was confirmed by x-ray examination of the stomach; two were discovered at operation, one was discovered at autopsy and one patient with only a tentative diagnosis died without confirmation. The primary lesion in ten cases was located in the stomach in two, the pancreas in two, the adrenal gland in one, the sigmoid in three and the ovary in two. One of the early cases (a man in his fifties) had been in the hands of several very good men. The patient's only symptom was mild intestinal and urinary disturbance. Primary carcinoma had been diagnosed by a cancer specialist and radium therapy was advised. Examination of tissue from the rectal wall and prostate was negative for carcinoma. At autopsy a small scirrhous carcinoma was found in the stomach. In a man of 21 the rectum was practically occluded by a large mass protruding into the anterior rectal wall. At operation implants were found from the bladder to the diaphragm. Tissue examination revealed teratoma of the adrenal. As a rule, biopsy from the rectal tissue does not show carcinoma, because only the superficial tissue is obtained. In ten of the twelve cases the infiltration of the rectal wall was annular and in two cases localized. In one of the cases of primary ovarian carcinoma a polyp at 4 inches in the rectum showed adenocarcinoma. Although these lesions are not of frequent occurrence, probably more would be found if a rectal examination were made in all cases of carcinoma of the abdomen. In my own experience only twelve secondary or extrarectal growths have been found as compared to 437 primary carcinomas. Treatment in these cases is at best only palliative.

DR. HENRY L. BOCKUS, Philadelphia: I am sorry that the audience has not been greater to hear Dr. Bacon's paper, because I feel that there are a good many of us who are not familiar with Blumer's shelf. I say that advisedly, coming in contact with students from all over the country, very few of whom have heard of Blumer's shelf when they arrive. It is a rather important thing to know that in carcinoma of the upper part of the abdomen there are a few locations that one should go over rather carefully for the possibility of metastases. It is my routine to feel above the left clavicle, in the left axilla, not forgetting to go deep under the pectoralis muscle, where the so-called Irish node is located, carefully palpate the umbilicus for any suggestion of a malignant growth, feel along the margin of the right rib to eliminate a malignant condition of the liver and feel the rectum on the anterior wall for a nodule or hard fibrotic shelf with a soft velvety mucosa over it. That is a Blumer shelf and in 95 per cent of the cases that means malignant infiltration. Dr. Bacon didn't mention another cause for such a shelf. I have reference to abdominal tuberculosis with secondary inflammatory changes and fibrosis. The incidence of Blumer's shelf in a malignant condition in the upper part of the abdomen is comparatively rare. I believe there are not more than two or three in a graduate hospital each year, but in a service at the Philadelphia Hospital, which I believe Dr. Bacon has, I believe many more would be found, because in the last stage of this condition Blumer's shelf is not too infrequent. I should like to mention another fact and that is that Blumer's shelf may constitute the first lead to a correct diagnosis. Any patient in whom a malignant growth is suspected should have a careful rectal examination to eliminate Blumer's shelf. Most of my patients in whom a shelf was palpated through the rectal wall have come with a diagnosis of cancer of the rectum.

DR. A. H. AARON, Buffalo: When one realizes that about 60 per cent of all the malignant lesions of the large intestine are within the reach of the examining finger and there is no field of malignancy that offers such great prognostic value as to cure, it is evident that this should be a routine measure in physical examinations. As to the various metastatic nodes, such as the Ewald node in the left supraclavicular region, Irish's node in the axilla and Straus's shelf (Blumer) in the pelvic floor, a better term can be applied; they are sentinel nodes, outposts demonstrating the presence of a malignant condition elsewhere in the body.

DR. HARRY E. BACON, Philadelphia: I am appreciative of this discussion. Dr. Bockus is quite right in saying that Blumer's shelf is found invariably in the late cases. Age, however, does not seem to play a great part.

A NEW AND FUNCTION-RESTORING OPERATION FOR BILATERAL ABDUCTOR CORD PARALYSIS

PRELIMINARY REPORT

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In presenting a new operation for the relief of bilateral cord paralysis, it seems fitting first to discuss the general principles involved in operations previously done for that purpose. All previous attempts to relieve the condition can be classified under four general headings.

This discussion is limited to a consideration of those bilateral recurrent nerve paralyses which follow operations for goiter. I have made no study of postdiphtheritic paralyses or those that occur as a part of the picture of progressive bulbar paralysis.

1. Permanent tracheotomy with insertion of a tube or with suture of the skin to the incised edges of the trachea so as to leave a permanent opening.

2. Nerve suture. The following nerves have been anastomosed to the distal portion of the injured recurrent nerve: (*a*) the proximal portion of the recurrent nerve, (*b*) the descendens noni, (*c*) the roots of the spinal accessory nerve and (*d*) the phrenic nerve.

3. Cordotomy or cordectomy either by punch operation or by laryngotomy with excision of one cord. This group of operations includes ventriculocordectomies, of which there are many modifications.

4. Cord displacements. These include all operations which are designed to displace one cord in a fixed outward position. Attempts have been made to split the thyroid cartilage and separate the anterior ends of the vocal cords by interposition of a piece of bone or cartilage. Others seat the anterior end of one cord in an outward position on the thyroid cartilage. Another creates a fixed outward displacement of one arytenoid cartilage.

No one of these operations has been productive of satisfactory results. The object of any operation should be to restore the functions of phonation and respiration.

Many of those devised were doomed to defeat in one or both of these objectives because of the very nature of the method chosen for attacking the problem. A brief discussion of the foregoing groups of operations will aid in a better understanding of the one subsequently described.

Tracheotomy has functioned more uniformly and satisfactorily than any other method. No one wants to wear a piece of plumbing in his windpipe, and at best a tracheotomy tube is a nuisance, though many patients are grateful for the relief so obtained. The desire to get away from the tracheotomy tube has been the father of all operations devised for the relief of bilateral abductor cord paralysis. That holds for the one herein described.

Nerve anastomosis would be ideal were it possible of success, as it would restore the functions of both phonation and respiration. Charles H. Frazier,[1] Sir Charles Ballance,[2] Frank H. Lahey [3] and others have written on the subject, but so far the results reported do not justify the adoption of that method of treatment as a standard procedure. For reasons later to be discussed, nerve suture will probably fail to secure good functional results even though nerve pathways are reestablished.

Cordotomies, cordectomies and cord displacements all have the same objections. It is not possible to alter permanently the position or physical structure of a vocal cord without creating a permanent change in the tone and quality of the voice. One might as reasonably remove the strings from a violin and replace them with hemp rope and expect it to produce the same tone and quality of sound as to cut out a vocal cord and expect the patient so deprived to speak in a normal manner. Sufficient air may be gained, though it is of necessity gained at the expense of the voice.

The operation I have developed is a new approach to the subject. The idea was borrowed from the procedures and practices of orthopedic surgeons. In principle it is based on the methods they use in dealing with motor nerve paralyses, whether they are of traumatic, toxic or infectious origin. I saw such surgeons transpose the tendons of functioning muscles to replace those of paralyzed muscles in the feet of children who were the victims of infantile paralysis. Some of those children were greatly benefited. The idea occurred to me that the same principle might be applied to the paralyzed vocal cords. This new approach is simple in its mechanics, physiologic in principle, and, furthermore, has worked with the patients operated on.

In order to understand it comprehensively, one must have a general knowledge of the mechanics of the larynx, its anatomy and all its functions as to both respiration and phonation, plus a knowledge of its action during deglutition.

The suprahyoid and infrahyoid groups of muscles are intimately concerned in all the functions of the larynx. Therefore a knowledge of them, their actions and their nerve and blood supply is also important. (Negus's [4] monograph more comprehensively covers laryngeal function than anything else in medical literature.) Briefly, the suprahyoid muscles pull the larynx upward during the act of swallowing. These muscles are the digastric, geniohyoid, geniohyoglossus, mylohyoid, stylohyoid and middle constrictor of the pharynx. Opposing that group is the infrahyoid group, comprising the sternohyoid, sternothyroid, thyroidhyoid and omohyoid. Their function is to counter the action of the suprahyoid group and to pull the larynx downward, partly as an aid in swallowing after the food bolus has entered the esophagus. Also they hold the larynx down and slightly depress it during inspiration. The mechanism of the larynx, which prevents foreign substances from entering it during swallowing, operates simultaneously with the suprahyoid group.

It is interesting that the suprahyoid and infrahyoid groups of muscles are both voluntary and involuntary in their actions. One swallows and breathes voluntarily; one also swallows and breathes involuntarily.

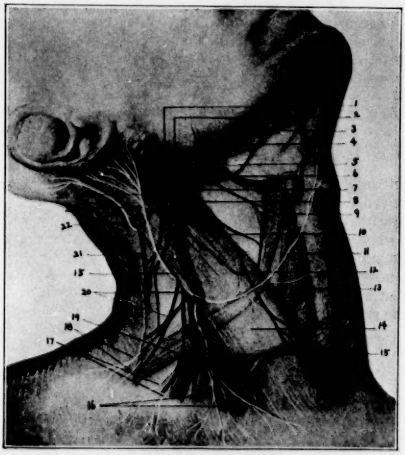

Fig. 1.—Nerve supply to the omohyoid muscle. (Figures 1 and 2 are reproduced from Callandar, C. L.: Surgical Anatomy, Philadelphia, W. B. Saunders Company, 1933.) 1, ramus marginalis mandibulae nervi facialis; 2, vena facialis posterior; 3, vena submentalis; 4, vena facialis anterior; 5, nervus hypoglossus; 6, vena auricularis posterior; 7, vena facialis communis; 8, vena jugularis interna; 9, musculus omohyoideus; 10, ramus descendens nervi hypoglossi; 11, nervus cutaneus colli; 12, nervus ansa hypoglossi; 13, vena jugularis anterior; 14, musculus sternocleidomastoideus; 15, vena jugularis externa; 16, nervi supraclaviculares anteriores; 17, nervi supraclaviculares medii; 18 nervi supraclaviculares posteriores; 19, plexus brachialis; 20, trunks of supraclavicular nerves; 21, ramus externus nervi accessorii; 22, nervus occipitalis minor; 23, nervus auricularis magnus; 24 nervus cervicalis III; 25, arcus venosus jugularis.

The function of the omohyoid muscle is opposition to the suprahyoid group. This muscle also assists in depressing the hyoid bone and larynx on inspiration. It therefore contracts automatically on inspiration as a part of its involuntary function. Gray [5] stated that "the omohyoidei not only depress the hyoid bone, but carry it backward and to one or the other side. They are concerned especially in prolonged inspiratory efforts."

The success of the operation herein described is primarily due to the previously developed habit of this muscle to contract automatically during inspiration.

1. Frazier, Charles H.: Anastomosis of the Recurrent Laryngeal Nerve with the Descendens Noni, J. A. M. A. **83**: 1637 (Nov. 22) 1924.

2. Ballance, Sir Charles, and Barnes, E. B.: Anastomosis of Recurrent Laryngeal Nerves to Phrenic Nerves: Some Recovery of Function, Brit. M. J. **2**: 158 (July 30) 1927. Ballance, Sir Charles: Results Obtained in Some Experiments in Which the Facial and Recurrent Laryngeal Nerves Were Anastomosed with Other Nerves, Brit. M. J. **2**: 349 (Aug. 30) 1924.

3. Lahey, Frank H., and Hoover, Walter B.: Injury to Recurrent Laryngeal Nerve in Thyroid Operations, Ann. Surg. **108**: 545 (Oct.) 1938.

4. Negus, V. E.: The Mechanism of the Larynx, St. Louis, C. V. Mosby Company, 1929.

5. Gray, Henry: Anatomy of the Human Body, Philadelphia, Lea & Febiger, 1924.

A complete discussion of the mechanics of the vocal cords is beyond the scope of this article; however, an understanding of their actions is necessary for a proper conception of what is to be accomplished in the operation. Briefly, the cords are adducted by the interarytenoideus, the thyro-arytenoideus and the crico-arytenoideus lateralis muscles. They are abducted by the crico-arytenoideus posticus muscles. They are tensed by the cricothyroid muscles. All these muscles except the cricothyroid are supplied by the recurrent laryngeal nerves. The cricothyroid is supplied by the external branch of the superior laryngeal nerve. There is a dispute among anatomists regarding the nerve supply to the interarytenoideus muscles. Berlin and Lahey reported anatomic dissections of the internal division of the superior laryngeal nerve showing fibers entering the interarytenoideus muscles. Lemere [6] concluded that these fibers are sensory and are merely passing through the muscles en route to the mucous membrane of the larynx. His conclusions are drawn from experiments on dogs, from human dissections and from taking 2,000 serial sections of the larynges of two babies, staining them for nerve fibers and thus reconstructing the course of the nerves. He stated that the nerve fibers do not end in the muscle but pass on through to the mucosa of the larynx.

From clinical observations, I lean to the theory that the internal division of the superior laryngeal nerve is purely sensory and that all the motor fibers of the nerve are carried by the external division which supplies the cricothyroid muscle. I have examined the larynges of nearly 100 patients who had recent unilateral cord paralysis and in no instance have I observed the slightest motion in a recently paralyzed cord or of the arytenoid cartilage to which it is attached. It would seem that if the interarytenoideus muscle was supplied by the superior laryngeal nerve, there would be a voluntary

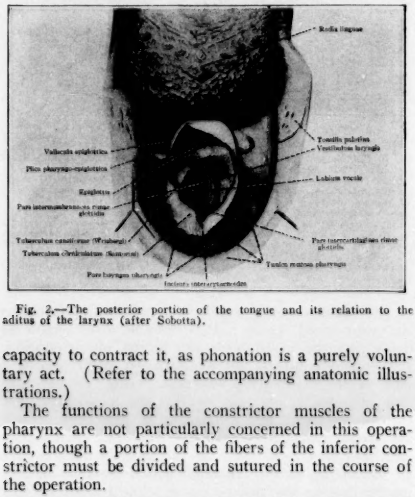

Fig. 2.—The posterior portion of the tongue and its relation to the aditus of the larynx (after Sobotta).

capacity to contract it, as phonation is a purely voluntary act. (Refer to the accompanying anatomic illustrations.)

The functions of the constrictor muscles of the pharynx are not particularly concerned in this operation, though a portion of the fibers of the inferior constrictor must be divided and sutured in the course of the operation.

6. Lemere, Frederick: Innervation of the Larynx: III. Experimental Paralysis of the Laryngeal Nerve, Arch. Otolaryng. **18**: 413 (Oct.) 1933; IV. An Analysis of Semon's Law, Ann. Otol., Rhin. & Laryng. **43**: 525 (June) 1934.

Preliminary tracheotomy should always precede this operation. A period of from four to six weeks is sufficient for the patient to become adjusted to the presence of a tracheotomy tube and for infection to be cleared.

An incision from 2½ to 3 inches long down the anterior border of the sternomastoid muscle is made, passing through the skin and platysma muscle. The tissues between the sternomastoid and the lateral wall of the thyroid cartilage are separated. This will bring the omohyoid into view. The inner border and posterior surface of the anterior belly of the omohyoid are dissected free. The outer border is carefully avoided except for a distance of three-fourths inch nearest to its attachment to the hyoid bone. Branches of the descendens hypoglossi enter the outer border, also its blood supply. It is very important to avoid injury to these. The muscle is then ligated with silk or chromic catgut from one-half to three-fourths inch below the hyoid bone. The muscle is unfortunately too long to exert traction on the arytenoid cartilage unless shortened to the proper length. Its tendonous attachment to the hyoid bone cannot be used for attachment to the arytenoid cartilage because of the excessive length of the muscle. The sheath of the muscle is so thin that it offers little support to sutures. This problem was met by ligating the muscle belly with chromic catgut about three-fourths inch below the hyoid bone and dividing the muscle distally to the ligature. The ligature thus creates a cuff behind which sutures hold in a satisfactory manner.

Fig. 3.—Hyoid bone, thyroid cartilage and external ligaments and muscles of larynx. (Figures 3, 4, 5 and 6 are reproduced from Barnhill, J. F.: Surgical Anatomy of the Head and Neck, Baltimore, William Wood & Co., 1937). 1, epiglottis; 2, 2, superior horns of hyoid bone; 3, 3, lesser horns of hyoid muscle; 6, omohyoid muscle; 7, sternohyoid muscle; 8, 9, 10, fasciculi of thyrohyoid ligament; 11A, exit of lymphatic trunk from larynx; 11, exit of vein from hyoid bone; 4, body of hyoid bone; 5, thyrolarynx; 12, entrance of superior laryngeal nerve; 13, entrance of internal branch of superior laryngeal artery; 14, thyroid notch; 15, 15, wings of thyroid cartilage; 16, 16, fasciculi of inferior constrictor muscle; 17, 17, cricothyroid muscles; 18, cricothyroid membrane (middle cricothyroid ligament); 19, cricoid cartilage.

Future experience may prove that it would be better to deal with this problem in stages, the first of which would be to bury the cut end of the muscle in the cervical fascia for a few weeks, until a new tendonous end was developed, and then transpose that to the arytenoid cartilage for attachment. There are other possible solutions of the difficulty.

There is a space of about 1½ inches along the outer border of the thyroid cartilage in which no important structure is to be encountered. It extends from the tip of the superior cornu of the thyroid cartilage to the inferior cornu. Above the tip of the superior cornu

there is danger of injury to the internal division of the superior laryngeal nerve. At the inferior cornu there is danger of injury to the external division of the same nerve. Along the border of the thyroid cartilage are to be found the attachments of the inferior constrictor of the pharynx. These fibers must be cut. The esophagus is then exposed. The wall of the esophagus in the region immediately behind the larynx does not appear to contain either circular or longitudinal fibers, and care must therefore be exercised in separating it from the posterior surface of the cricoid cartilage.

The arytenoid cartilages articulate with the cricoid on its posterior and outer borders. They, with the cartilages of Wrisberg and Santorini, act like corset stays in a rather thin wall that separates the openings of the larynx and esophagus. The arytenoid cartilages sit on a facet-like joint and extend upward for about one-half inch. The esophagus must be separated from the posterior spinous border of the arytenoid cartilage. In this dissection, one must be careful to avoid making an opening into either the esophagus or the larynx. The muscular process of the arytenoid cartilage will be exposed in this maneuver. Immediately beneath the muscular process is the facet-like joint. This, like any joint that has been immobilized for years, is stiff and its ligamentous capsule contracted. I have found it advisable to mobilize the arytenoid cartilage by cutting the ligamentous capsule of its joint on three sides, the mesial, the outer and the posterior, the last of which also divides the atrophic fibers of the crico-arytenoideus posticus muscle.

The posterior border of the arytenoid cartilage is then scraped clean and the cuffed end of the omohyoid attached to it by silk sutures which pass through both the muscle and the arytenoid cartilage. In the aged, the cartilages of the larynx become ossified, rendering it difficult to pass a needle through the arytenoid without fracturing the cartilage. This occurred in the second case here reported. It is interesting to note that this patient secured the best result of any on whom the operation has been performed.

The cut fibers of the inferior constrictor of the pharynx are then sutured. This leaves the omohyoid passing through an aperture in the inferior constrictor. The platysma is closed with two or three interrupted catgut sutures and the skin with clips.

COMMENT

When the idea of this operation was first conceived, I thought that it should be applied to only one cord. This conclusion was based on the fact that patients with one cord paralyzed generally do not suffer much disability in either phonation or respiration. The paralyzed cord usually comes to rest in or near the midline position, which is the position of phonation. The opposite cord is thus able to approximate it on phonation and also open the larynx on respiration. If sufficient airway has been obtained by operating on one cord, there is no occasion to repeat the operation on the opposite cord. If for any reason the desired result is not secured in a given case, there can be no objection to operating on the opposite side.

Examinations of the second patient on whom this operation was performed revealed some very interesting results. The operation was done on the left side. Two weeks later the left cord was observed to open automatically on inspiration. Furthermore, there was some capacity to adduct the cord at that time. At the end of seven weeks there was sufficient abduction of the cord to permit the removal of the tracheotomy tube. The patient can adduct the cord as well as the normal person. It is more than three months since the omohyoid was transposed to the arytenoid cartilage. The tracheotomy wound has been closed for a month. The patient can talk and breathe practically as well as the normal person, has gained 16 pounds (7 Kg.) and states that she can now comfortably eat and breathe at the same time. Her cords are easily visualized with a laryngeal mirror.

It is easy to understand her capacity to open the cord, but the ability to adduct it is a point about which there may arise a difference of opinion. I am of the

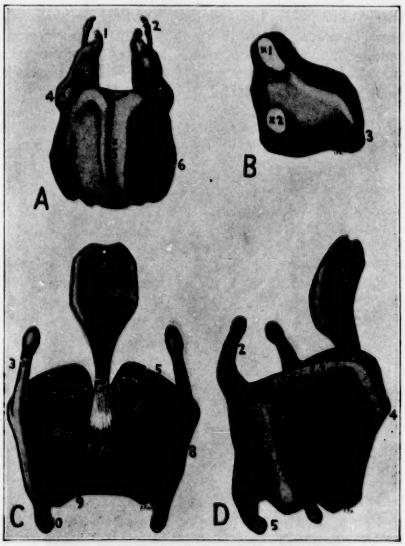

Fig. 4.—*A*, posterior view of cricoid and arytenoid cartilages: 1, corniculate cartilage; 2, cuneiform cartilage; 3, arytenoid cartilage; 4, muscular process of arytenoid cartilage; 5, median ridge, posterior surface of cricoid cartilage; 6, lateral view of cricoid cartilage. *B*, lateral view of cricoid cartilage (note wide posterior portion, making a completed ring): 1, facet for articulation with arytenoid cartilage; 2, facet for articulation with lower horn of thyroid cartilage; 3, anterior part of cricoid ring. *C*, thyroid cartilage from behind, showing interior surface: 1, epiglottis; 2, pits for glands in epiglottis; 3, superior cornu of thyroid cartilage; 4, ligament of epiglottis; 5, superior rim; 6, interior surface of thyroid cartilage; 7, site for anterior attachment of true and false vocal cords; 8, posterior margin of cartilage; 9, inferior margin; 10, inferior cornu. *D*, lateral view of thyroid cartilage: 1, epiglottis; 2, superior cornu; 3, superior margin; 4, notch of thyroid cartilage; 5 inferior horn.

opinion that neither the interarytenoideus muscles nor the intrinsic muscles of the cord are necessary to produce adduction and tension of the cord under the conditions prevailing in this case. Evidently the faculties of adduction and tension of the cord are produced in this instance by the cricothyroid muscles, which are supplied by the superior laryngeal nerves, plus the contracted interarytenoideus fascia. However, the cricothyroid muscles are not capable of producing adduction or tension of a cord that has recently been paralyzed. This difference in action is presumably due to the fact that with recent nerve injury the cord is flaccid while with an old injury it is taut and contracted, so that when the cricoid cartilage is tilted backward,

further tension on the cord shifts it into the midline (fig. 3). Stridor, which was pronounced in this case prior to operation, is entirely absent, even on deep inspiration. The patient's family states that prior to the operation during sleep she disturbed the entire household with the most terrifying choking noises and that she now sleeps without noise.

Patients who are wearing tracheotomy tubes are in one sense ideal for the operation of muscle transposition, as the presence of the tracheotomy tube eliminates the first stage. For reasons to be mentioned later, long-standing bilateral paralysis presents a different problem from recent paralysis. In recent paralysis the cords are in an outward position, with the arytenoid cartilages widely separated. This state prevails only for from three to six months. In long-standing paralysis, the cords are contracted and shortened. The interarytenoideus muscles and fascia have become contracted and the arytenoid cartilages drawn much closer together than in recent paralysis.

I have not seen an adequate or accurate description of the composite picture of the glottis, the larynx, the aryepiglottic folds, the arytenoid cartilages and the vocal cords such as exists in cases of long-standing bilateral recurrent nerve paralysis. It can readily be demonstrated by motion pictures of the larynges in such cases in comparison with normal larynges. It is apparent by the simple observations made with an ordinary laryngeal mirror. There is considerable variation in normal human larynges. For example, the male adult larynx is from 8 to 10 mm. greater in its average anteroposterior diameter than the adult female larynx.

Fig. 5.—Anteroposterior section of larynx, showing left half. Mucosa has been removed from muscles. The superior and recurrent laryngeal nerves are shown supplying the internal muscles. 1, superior laryngeal nerve; 2, external branch; 3, internal branch; 4, superior horn of thyroid cartilage; 5, main branch of internal laryngeal nerve; 6, epiglottis; 7, 8, corniculate cartilages; 9, 9, cut edge of thyroid cartilage midline; 10, 10, cricothyroid muscle; 11, branch of recurrent nerve entering arytaenoideus posticus; 12, section of esophagus behind cricoid cartilage; 13, 13, rings of trachea; 14, recurrent laryngeal nerve. A branch of recurrent laryngeal nerve is shown entering crico-arytaenoideus posticus. Immediately above the crico-arytaenoideus posticus the recurrent nerve enters the crico-arytaenoideus lateralis, and just above the latter it enters the thyro-arytaenoideus. Only the external branch (2) of the superior laryngeal nerve enters any muscle. All other branches go to the mucosa and are cut off, as shown. The recurrent nerve (14) supplies all the intrinsic muscles except the cricothyroideus (10).

With the idea of trying to get a better composite picture of all the changes that occur in the larynx after bilateral recurrent nerve paralysis, I recently examined the larynges of five patients. There is an apparent narrowing of the lateral diameter of the larynx. The arytenoid cartilages are fixed in close approximation and lean more forward than normal. The entire glottic opening seems more oval than in the normal larynx. The sphincteric mechanisms of the larynx (the component parts of the mechanism of the so-called epiglottic reflex) are all seen to be in a contracted state. This mechanism is made up of the epiglottis, the aryepiglottic folds, which are supported by the cartilages of Wrisberg and Santorini and the arytenoid cartilages, and the interarytenoideus fascia and muscles, combined with the false and true cords. These structures act as a sort of elastic cuff surrounding the opening of the larynx. They are a portion of the defensive mechanism which protects the larynx against the entrance of foreign substances. In conjunction with the suprahyoid muscles, which draw the larynx up behind the base of the tongue, they act to close the larynx during deglutition. The epiglottis does not close the larynx like a trap door. It is only one of several structures that protect the larynx during the act of swallowing.

Fig. 6.—Posterior view of larynx and upper part of trachea. Some of the intrinsic muscles are shown. A study of these muscles, their attachments and the laryngeal cartilages will give a good understanding of the muscular function. 1, epiglottis, running downward and backward, from which on either side is the airy epiglottis ligament (the little swellings on this ligament indicate the position of the cuneiform and corniculate cartilages); 2, superior cornu of thyroid cartilage; 3, inner surface of thyroid cartilage; 4, 4, 4, arytaendoideus, showing different direction of its fibers; 5, posterior surface of cricoid cartilage; 6, crico-arytaenoideus posticus; 7, upper tracheal rings.

Thinking in terms of what happens in motor nerve paralyses of the extremities, one has only to go back to the initial symptoms of bilateral recurrent nerve paralysis in order to predict accurately what is ultimately going to develop in the larynx.

The initial symptoms of bilateral recurrent nerve paralysis are loss of voice and loss of epiglottic reflex. The former means paralysis of the muscles of phonation and the latter paralysis of the muscles of the defensive mechanism of the larynx. The patient can only whisper, and any effort to swallow fluids results in a portion of the fluid entering the larynx; it is immediately expelled and effort to swallow is temporarily abandoned.

If a patient dies in the first few days following such injury, death is usually due to drowning in his own secretions or to pneumonia of a foreign substance type. The defensive mechanism of the larynx returns to function more quickly than that of phonation. It is more primitive in origin and also is aided by the suprahyoid group of muscles, which are not affected.

These symptoms can have only two interpretations: 1. There is paralysis of the muscles of phonation. 2. There is paralysis of the laryngeal defensive mechanism, the inevitable consequences of which are (*a*) flaccid paralysis, (*b*) atrophy, (*c*) fibrosis and (*d*) contractures. That is exactly what happens in both the vocal and the defensive mechanisms and that is why the term bilateral abductor cord paralysis does not fit the situation.

The arytenoid cartilages are the gates that open and close the larynx. They act as sliding doors in the cuff that surrounds the laryngeal orifice. Furthermore, they have attached to them the vocal cords, which open and close with the gates. If one thinks of this sliding door effect as operating on a circular base like a roll top desk, the picture becomes more clear. In long-standing bilateral nerve paralysis, they have become locked together by the interarytenoideus muscles and fascia, which have become contracted as a part of the general contractures that take place in all the elements of the sphincteric mechanism of the larynx. Not only that, but the base on which the sliding doors operate has become rusted and frozen, so to speak.

As a result of this locking together of the arytenoid cartilages, I have noticed a tendency in the first and third patients operated on for both cartilages and both vocal cords to be drawn to the same side by the pull of the omohyoid muscle. This condition of affairs presented a problem that I had not foreseen. Incidentally, it is a problem that the advocates of nerve suture have not foreseen. Even if nerve regeneration were to take

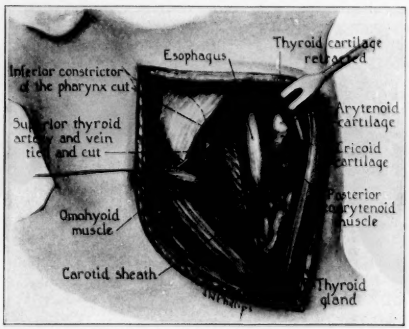

Fig. 7.—The inferior constrictor of the pharynx cut and the superior thyroid artery and vein tied and cut.

place following nerve anastomosis, this problem would still be present, and it is improbable that the crico-arytenoideus posticus muscles could develop strength enough to deal effectively with it. Nerve regeneration could not be expected to take place in less than six months and probably would not occur in less than one year. It is in that period that the fatal contractures enumerated take place.

This is a purely mechanical problem and one that must be solved by purely mechanical principles. With long-standing paralysis one must consider doing a reconstruction of the glottic opening. If the sliding gates of a barnyard are tied together with rope, the simplest method of dealing with the problem is to cut the rope. The same thing can be done with the inter-arytenoideus muscles and fascia. If the track on which

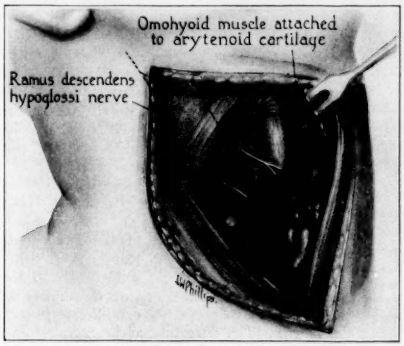

Fig. 8.—The omohyoid muscle attached to the arytenoid cartilage.

those gates slide has become rusty and the wheels are frozen, it must be cleaned and oiled. If the capsule surrounding the crico-arytenoid joint has become contracted and the joint frozen, it must be divided to permit the cartilage to slide outward.

After the interarytenoideus muscle and fascia have been divided and the joint capsule severed, it would seem important to displace temporarily the arytenoid cartilage outward as a means of preventing the recurrence of contracture by new-formed scar tissue. This can be accomplished by drilling a hole in the posterior border of the thyroid cartilage at the proper level and then passing a chromic catgut suture through this hole and through the arytenoid cartilage. When this suture is tied, it will temporarily anchor the arytenoid cartilage in an outward position. During the period required for the absorption of the catgut suture, opportunity is provided for the omohyoid to take over the task of future abductions of the cartilage. The operation of the foregoing ideas is somewhat speculative. If proper care is exercised in putting these suggestions into effect, no harm can be done. I believe it quite possible that better results may be obtained by following them. The omohyoid is a much stronger muscle than the crico-arytenoideus posticus and therefore can exert more powerful pulls on the cartilage.

In cases of recent recurrent nerve paralysis, the arytenoid cartilage is found to be in an outward position. The cord is also in an outward position, and the sphincteric mechanism of the glottis has not become contracted. If the foregoing reasoning is rational, it would seem that the ideal time for muscle transposition is as early as possible. The idea is to get the omohyoid into operation before contracture has taken place. In cases of peripheral nerve lesions, orthopedic surgeons begin at once to apply counter measures to prevent contractures. Those methods are splinting in positions of function and passive motion. There is no conceivable means of applying splinting or passive motion to the

muscles of the larynx. Therefore the question of time becomes tremendously important in dealing with motor nerve injury to the larynx. Motor nerve injury to the muscles of the larynx is no different in fundamental principle from motor nerve injury to the muscles of the arm, leg or other part. The principles that have proved helpful in the one should be beneficial in the other.

Every surgeon is familiar with the course of events following peripheral motor nerve paralysis. It is the same in all motor nerve paralyses. At first there is flaccid paralysis of the muscles and loss of power to contract and then atrophy, fibrosis and contracture. This is exactly what happens in the larynx. The term bilateral abductor cord paralysis is in reality a misnomer. It does not describe the conditions prevailing in the larynx. The surgeon has been accustomed to examining the vocal cords while forgetting the other structures in the larynx.

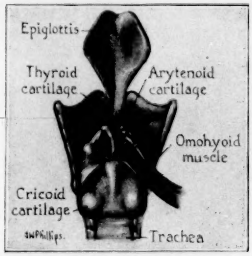

Fig. 9.—Procedure in cases of early involvement; reconstruction features omitted.

In the operation I have devised, effort has been made to follow as closely as possible recognized orthopedic procedures for the treatment of peripheral motor nerve paralysis. In the proposed plan of reconstructing the larynx in cases of long-standing paralysis and contractures, the methods of orthopedic surgeons have been modified only to fit different circumstances. In cases of old or neglected paralysis they divide stiff joint capsules, forcibly stretch others, cut contracting bands of fibrous tissue and splint extremities in positions of best function.

In dividing the crico-arytenoid joint capsule and in cutting the contracted interarytenoideus muscles and fascia, the same methods are used. In drilling a hole in the border of the thyroid cartilage and passing a catgut suture through it and through the arytenoid cartilage and tying it tightly enough to displace the cartilage outward, I am simply applying a temporary splint which will suffice to hold it in a position of respiratory function while the omohyoid is becoming attached in such a position that it will exert passive motion with each inspiration as long as the patient survives. The splint is absorbed in two weeks.

Immediate nerve suture is recognized as a correct course in cases of severed peripheral motor nerves. For the reasons previously mentioned, for the reason that complete restoration of function is seldom or never obtained, for the reason that the recurrent nerve is small, difficult to find and difficult to suture and for the additional reason that the recurrent nerve is supposed to carry adductor and abductor fibers in two separate cords within its sheath, proper hook-up of neurons is a remote possibility. Undoubtedly in these reasons is to be found the answer to the high percentage of failures following nerve suture.

In a case of recent bilateral nerve paralysis, what should be done? In the past the surgeon has sat on the sidelines and hoped and prayed a sort of sick-at-the-stomach prayer that in a few days or weeks everything would be all right. He has been delighted when in a few weeks the patient's voice began to return, only to sink to the depths of despondency when faced with the full facts of what has taken place.

From observations on the patients for whom muscle transposition has been done, I believe that the earlier it is done the better chance there is for a satisfactory result. It should require only a few days to determine whether or not real injury has occurred to both recurrent nerves. Just as soon as a decision can be made, a tracheotomy tube should be placed in the trachea, and as soon thereafter as is feasible muscle transposition should be effected. If the operation is done within the first three or four months following paralysis, reconstructive features should not be necessary, as contractures of a serious nature will not have developed. The omohyoid does not have to be trained to contract during inspiration. It does so automatically.

Occasionally nerve paralysis is only temporary. If, however, it is bilateral and has not cleared in two or three weeks and if stridor is present, the probability of recovery's taking place is quite remote. An experienced laryngologist could, in a majority of instances, predict with considerable accuracy what the course would be. Thus unnecessary operations could be avoided. Many operations for paralysis of the vocal cords must be performed in order for the surgeon to perfect a technic. Each case must be studied carefully prior to operation. The plan herein proposed for relatively recent involvement, plus the reconstructive features, should be applicable to all.

No one should undertake this operation without first acquiring an accurate knowledge of the anatomy involved. I suggest that any one who wishes to undertake it first go to an anatomic laboratory and do it, not once but several times. Don't send an assistant to the laboratory to learn the anatomy for you unless you plan to let the assistant perform the operation. No substitute for normal anatomy can be expected to function as well as normal anatomic structures. As a general rule, in doing reconstructive operations the closer one approaches normal functions the better are the results obtained.

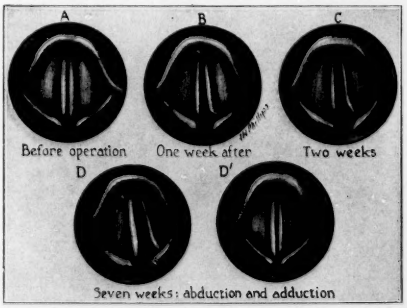

Fig. 10 (case 2).—The vocal cords in action.

I have studied about twenty cases of bilateral recurrent nerve paralysis but have not had an opportunity to follow any case from its inception. I examined one patient the day following bilateral nerve injury. She died the following day from diabetes and hyperthyroid crisis. The cords were in the cadaveric position. The

arytenoid cartilages were widely separated and yet she had stridor and loss of function of the defensive mechanism of the larynx.

Prior to examination in the other cases, the paralysis had existed from six months to seventeen years. The twenty patients will be grouped into three classes on the basis of what I have seen, not what I have read:

1. A group in whom the cords are so contracted and closely approximated that tracheotomy has been necessary in order to prevent suffocation.

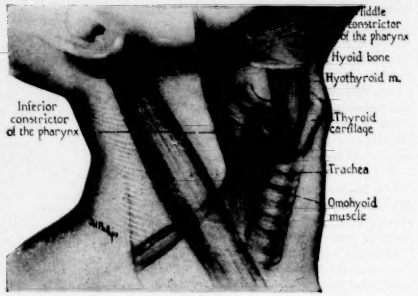

Fig. 11.—The new position of the omohyoid at the close of the operation.

2. A group in whom the cords are also closely approximated but who are able to survive by leading very inactive lives.

3. A group in whom the cords do not come to rest in a midline position but about halfway between the positions of phonation and respiration.

In the third group, I have seen two patients. They could speak fairly well. The voice was a bit husky and monotonous. They could get sufficient air for ordinary activities. It is probable that some laryngologists would classify their condition as partial paralyses. Both have sufficient airway to lead ordinarily active lives, and both have very slight adduction and abduction of the cords. Both have stridor and also respiratory embarrassment on exertion. Both had thyroidectomy followed by the usual symptoms of bilateral nerve paralysis, namely, complete loss of voice, inspiratory stridor and loss of epiglottic reflex; there was gradual improvement in the voice after several weeks, and as the voice improved dyspnea and stridor became more pronounced. It is difficult for me to conceive of an equal degree of bilateral partial nerve paralysis occurring as the result of surgical trauma. Therefore I classify them as having complete paralysis without the usual degree of contractures.

I am of the opinion that the entire conus elasticus is immediately involved in the flaccid state that follows the injury. The opinion is based on observations on the only patient I have seen within forty-eight hours after paralysis occurred. Her stridor was of a different quality from that in cases of old involvement. It was more fluttery, a sort of flapping in the breeze, so to speak, and not the high-pitched crowing sound that is present with old involvement. With a mirror, the cords were observed to be flaccid and widely separated, and the entire lining of the larynx seemed to vibrate on inspiration.

This opinion is supported by the fact that the muscular fibers of the conus elasticus are derived from external division of the thyro-arytenoideus muscle, as are the muscular fibers of the membrane quadrangularis (fig. 12), as shown by Negus.[4] It follows that the conus and membrane quadrangularis are involved in the flaccid state. The muscular fibers of these structures, being offshoots from the thyro-arytenoideus, are likewise supplied by the recurrent nerves.

It is probable that in the instances in which obstructive dyspnea has developed on the operating table immediately after bilateral paralysis, it has been due to the relaxed conus folding on itself, a sort of modified intussusception during strong inspiratory effort, rather than to contractures of the cords. The latter could not take place.

The musculi aryepiglottici (fig. 13) are offshoots of the interarytenoideus muscle. They contract in unison or as a part of the contractures of that muscle during both deglutition and phonation. These muscles are likewise supplied by the recurrent nerves. It is thus apparent that all the muscular structures of the larynx that are concerned in the acts of phonation and deglutition will be involved in, first, the flaccid state and, ultimately, the contracted state which follows bilateral recurrent nerve paralysis.

REPORT OF CASES

Three patients have been operated on with the method described. The complete technic of laryngeal reconstruction has not been used in any case, although a rather close approach to it was used in the second case. It has been worked out on the cadaver and will be tried and the results will be reported at a future time.

CASE 1.—Sister B., aged 42, who was operated on for exophthalmic goiter in 1921, had a loss of voice, which lasted a few months, and then shortness of breath and stridor, which persisted. Exercise caused marked respiratory embarrassment. She lost weight, and eating was difficult because of shortness of breath.

In 1933 she had a recurrence of the goiter, which was removed. She did not gain satisfactorily after the operation,

Fig. 12.—Note particularly the muscle fibers of conus elasticus and membrana quadrangularis. In recent paralysis these membranes are flaccid; later they are involved in the contractures. (Figures 12 and 13 are from Spalteholz, Werner: Hand Atlas of Human Anatomy, Philadelphia, J. B. Lippincott Company, vol. 3.)

and in the past two years dyspnea had increased and stridor become more pronounced. Stridor was pronounced during sleep.

The patient was small, weighing 100 pounds (45 Kg.). The pulse rate was 84, the heart and lungs were normal and the blood pressure was 132/76. The vocal cords were difficult to examine but were fixed in the midline position. Stridor was pronounced on inspiration. Physical examination revealed no other abnormalities.

Operation was performed July 20. One-fourth grain (0.016 Gm.) of morphine and 1/150 grain (0.0004 Gm.) of atropine were given one hour before operation. Nitrous oxide and oxygen anesthesia was used. The patient's condition immediately became so alarming, stridor so pronounced and cyanosis so marked that the trachea was exposed for the purpose of inserting a tube. The patient's condition improved somewhat, and tracheotomy was postponed for the last step, as opening

Fig. 13.—Note that the musculis aryepiglotticus is an offshoot of the interarytenoideus muscle.

the trachea would increase the chances of infection in the wound. At the close of the operation, the trachea was opened and a number five tube inserted.

For two reasons this was not a satisfactory surgical experience: 1. Inhalation anesthesia had proved dangerous and unsatisfactory. 2. The tracheotomy wound naturally became infected and exposed the adjacent wound to infection. It was therefore decided to seek a more satisfactory type of anesthesia and that no other patient would be operated on without a preliminary tracheotomy.

In the two subsequent operations, pentothal sodium (sodium ethyl [1 methyl butyl] thiobarbiturate) was used intravenously. It produced satisfactory surgical anesthesia. It has an additional advantage in that the anesthetist's equipment is far removed from the operative field. I have considered using local anesthesia. It would offer opportunity to observe the action of the omohyoid muscle on the arytenoid cartilage. It is a most intriguing thought. I have been afraid to undertake its use because of fear that the manipulations of the larynx would set up paroxysms of coughing, under which circumstance one could not work. Also I fear the possibility of a blowout in the uncovered portion of the esophagus during such paroxysm.

The postoperative course of this patient was uneventful. Six weeks after operation she expressed a desire to be rid of the tracheotomy tube, stating that when she placed her finger over the opening in the tube she could breathe through her mouth much more easily than prior to the operation. The tube was removed, and the wound closed in a few days. She taught school half days during November and December 1938. On the opening of school in 1939 she took a full day's work in a grade school. She has gained 9 pounds (4 Kg.), can go for a two hour walk without fatigue or respiratory embarrassment, has a good speaking voice, and except for a slight inspiratory stridor, which still persists, one would not casually be aware of any abnormality.

On account of an extremely sensitive gagging reflex, it has been difficult to examine her cords satisfactorily. By training this difficulty has been overcome to a degree where the opening and closing of her left cord can be observed (the omohyoid was attached to the left arytenoid cartilage). More symptomatic improvement has occurred during the month of December than in any other month following the operation.

CASE 2.—Mrs. S., aged 73, who was operated on for goiter eleven years before, had lost her voice except for a whisper for several months. When it began to return, difficulty in getting her breath developed. As the voice became stronger, respiration became more difficult. For the past ten years she had been more or less of an invalid. Going upstairs or up a slight grade was a laborious task on account of shortness of breath, and during the past year the symptoms had become worse. She had gradually lost 32 pounds (14 Kg.) and stated that it was difficult to eat and breathe at the same time.

The patient was of poor color and poor nutrition. The eyes were normal, the teeth artificial and the tonsils normal. A pyramidal lobe 1½ inches long and one-half inch wide, freely movable and extending up to the hyoid bone, was present. Pulsations in the carotid vessels were normal. In breathing there was the typical sound made by tracheal obstruction. The heart and lungs were normal. There was no tremor. The vocal cords were fixed in the midline position. The blood pressure was 142/70. Fortunately the vocal cords were easily visualized. They were contracted to almost complete approximation in the resting state and separated by a very narrow aperture on inspiration. She had marked stridor.

She was admitted to the hospital June 30, 1938. July 2 at 7 a. m. she was given one-fourth grain (0.016 Gm.) of morphine and 1/150 grain (0.0004 Gm.) of atropine hypodermically. She arrived in the operating room at 8 a. m. in such an extreme state of respiratory embarrassment with cyanosis and pronounced increase in stridor that tracheotomy was immediately done with local anesthesia and she was returned to her room. She went home on the fourth day. In two months she returned, her weight having increased from 113 to 129 pounds (51 Kg. to 58 Kg.) simply because she was able to eat and breathe at the same time.

The steps as previously described were caried out. Her arytenoid cartilage had become ossified, and in an attempt to pass a needle through it the upright portion was fractured.

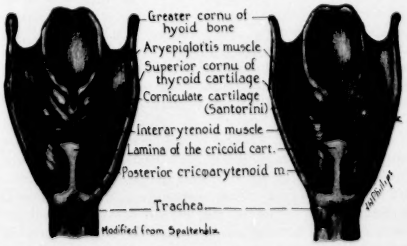

Fig. 14.—Severing the interarytenoideus muscle and fascia and anchoring the arytenoid temporarily to the thyroid cartilage.

It was a disturbing experience and I thought one calculated to defeat the purpose of the operation. However, a second suture was placed through the distal fragment and the muscle sutured to it.

A temperature of 102 F. developed on the fourth postoperative day, rising to 103.2 F. on the fifth day, and the patient showed signs of bronchopneumonia. On the following day the temperature dropped to 99 F., with a subsidence of symptoms, and recovery was speedy and uneventful.

These first two patients operated on belonged to group 2 of the preceding classification; the third belonged in group 1.

CASE 3.—Mrs. J., aged 63, who had been operated on ten years previously for goiter with a loss of voice and gradual return, had the usual stridor and dyspnea. At the end of eight months dyspnea had become pronounced; several choking spells had occurred, during which she had become cyanotic and unconscious. Tracheotomy was performed at that time, and she had worn a tube for nine years.

The results of physical examination were unimportant except in two particulars. Her cords were unusually tense and closely approximated. She was wearing the largest tracheotomy tube I have ever seen. By placing the finger over the opening of the tube, one immediately realized that she could not survive on the air intake through the larynx.

Operation was performed Dec. 2, 1938. The muscle was transposed in the manner previously described. The postoperative course was uneventful, and she was discharged in one week.

At the end of two weeks she reported that she could note no improvement. Examination of her cords revealed no change in position, there was no movement and moderate edema was present at the base of the left arytenoid cartilage. In three weeks she returned very happy and said that she had been able to smell food being cooked for the first time in nine years. She was also able to blow out a lighted match or a candle, which she had not previously been able to do. This meant, of course, that she was getting more air through the nose and mouth. (It is interesting that the first improvement noted by the second patient occurred at the end of two weeks, when she was able to blow her nose for the first time in eleven years.) At the end of five weeks, motion was developing in the left cord, but not sufficient to permit removal of the tube.

POSTOPERATIVE OBSERVATIONS

The difference between the margin of space separating the vocal cords that is sufficient to sustain life and that which is sufficient to sustain a person at ordinary activities is not great. Patients 1 and 2 have sufficient airway to sustain them at ordinary activities. Patient 3 has a good voice but as yet not sufficient airway. If in three or four months she has not been able to stretch the contractures so as to permit wide enough opening of the left cord for removal of the tracheotomy tube, the right omohyoid will be transposed and the contracted interarytenoideus muscle and fascia divided.

It was only after observing the progress in these cases and collecting others and comparing the larynges with normal ones that I realized that laryngeal reconstruction must accompany muscle transposition in order to succeed satisfactorily in all cases of long-standing involvement.

The operation in the second case was more successful than the others. In fact the patient has practically perfect restoration of the functions of phonation and respiration. Interestingly, a major portion of the atrophic fibers of the interarytenoideus muscle and fascia were separated from the left arytenoid cartilage in that case. No effort at such separation was made in the other two.

CONCLUSIONS

1. Transposition of the omohyoid muscle to the arytenoid cartilage in cases of recent bilateral recurrent nerve paralysis plus laryngeal reconstruction in cases of old involvement with contracture presents an entirely new approach to the solution of this perplexing problem.

2. Motor nerve paralysis of the larynx is not different in fundamental principle and pathologic changes from peripheral motor nerve paralysis in other parts of the body.

3. Recognized orthopedic and surgical procedures for peripheral motor nerve paralysis have proved beneficial in the treatment of laryngeal paralysis.

4. An accurate knowledge of laryngeal anatomy and function is necessary for success in these procedures. Bunglesome operations in this region are sure to bring both the operation and the operator into disrepute.

5. It is probable that persons now wearing tracheotomy tubes because of bilateral recurrent nerve paralysis can be relieved of that necessity and that others may be restored to active and comfortable lives.

6. Once a chordectomy, always a chordectomy. Therefore I believe chordectomies should be discontinued until the merits of muscle transposition and laryngeal reconstruction can be adequately evaluated.

7. It is too early to know what the final outcome of these operative procedures will be. It is not possible to draw final or statistical conclusions from three cases. The results so far justify their application to a sufficient number of patients for proper assay of the values. If in the future other patients are benefited to the same degree as the patients here reported on, the nightmare of bilateral nerve paralysis will have been plucked of most of her gray hairs.

812 Medical and Dental Building.

FATAL GRANULOCYTOPENIA FOLLOWING ADMINISTRATION OF SULFANILAMIDE

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AND
A. E. PRICE, M.D.
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Nine cases of fatal granulocytopenia due to sulfanilamide preparations have been reported. Four of these cases came to autopsy and in two instances the bone marrow was studied. An additional fatality with conditions found at autopsy and on study of the bone marrow is here presented.

REPORT OF CASE

J. D., a white man aged 45, was admitted to the William J. Seymour Hospital May 31, 1938, because of a recurrent left inguinal hernia which had been present for twenty-five years, pain in the left groin of one year's duration, and a chronic cough productive of whitish sputum for fifteen years. A chancre twenty-five years before was followed by treatment with numerous injections of arsphenamine and mercury. The admission diagnosis was left indirect inguinal hernia, postoperative herniorrhaphy adhesions, chronic bronchitis and latent syphilis.

June 15 the patient was operated on for a left indirect inguinal hernia. The postoperative course was uneventful until June 25, when the patient experienced sudden, severe, knifelike pain in the right side of the chest anteriorly, associated with difficulty in breathing. Physical examination revealed a diminution of breath sounds over the left base and right lower lobe and impairment of the percussion note over the right base posteriorly. The temperature was 100 F., the pulse rate 110 and the respiratory rate 20. The following diagnoses were considered: early pneumonia, pulmonary infarction and pulmonary atelectasis. The following day the temperature rose to 102 F. and the sputum was positive for pneumococcus type II. Sulfanilamide 120 grains (8 Gm.) was given followed by 20

From the Departments of Pathology and Medicine, Dr. William J. Seymour Hospital.
The pathologic studies and diagnoses were made with the assistance and confirmation of Dr. S. E. Gould, chief of the department of pathology of Eloise and Seymour hospitals.

grains (1.3 Gm.) every four hours. The next day, June 27, the sulfanilamide level of the blood reached 13.6 mg. per hundred cubic centimeters. Culture of the blood yielded negative results. Films made on a portable x-ray machine showed no consolidation.

The patient's condition showed no change until July 2, when his temperature rose to 104 F., the pulse rate to 120 and the respiratory rate to 50. On this date the sulfanilamide level was 5.6 mg. per hundred cubic centimeters of blood. The following day the patient appeared critically ill with dyspnea, cyanosis, stupor and profuse sweating. Breath sounds were diminished and tactile fremitus increased at both bases posteriorly. July 5 the patient was put in an oxygen tent. The blood count showed a hemoglobin content of 11.5 Gm., erythrocytes 4,010,000, leukocytes 13,450, polymorphonuclear leukocytes 77 per cent, lymphocytes 16 per cent and monocytes 7 per cent. July 7, medseen), monocytes 4 per cent, and eosinophils 2 per cent. Capillary fragility (tourniquet) test produced no petechiae. A smear of aspirated sternal bone marrow showed lymphocytes 49 per cent, eosinophils 1 per cent, basophils 1 per cent, eosinophilic myelocytes 1 per cent, blast forms 1 per cent, normoblasts 43 per cent, megaloblasts 4 per cent and polymorphonuclear leukocytes 0.2 per cent. The patient was given 10 cc. of pentnucleotide and 2 cc. of liver extract twice a day and in addition a transfusion of 600 cc. of citrated blood was given. Two days later administration of pentnucleotide (10 cc.) was increased to three times a day. Blood transfusions were given daily. July 16 a small ulcerative lesion was first noticed on the tip of the tongue. This lesion spread to the mid region of the tongue the next day. The patient died the morning of July 18 with a temperature of 107.8 F., a pulse rate of 140 and a respiratory rate of 50.

TABLE 1.—*Blood Counts and Free Sulfanilamide Blood Values*

Date, 1938	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Polymorphonuclears	Filamentous	Nonfilamentous	Lymphocytes	Monocytes	Basophils	Eosinophils	Blood Sulfanilamide, Mg. per 100 Cc.	Comment
6/ 1	14.5	4.95	6,300	.....	77	62	13	10	13	..	..	....	
6/25	15.5	4.98	15,200	.....	..	..	..	..	..	..	..	....	
6/26	....	....	.....	.....	..	..	..	..	..	..	..	....	Sulfanilamide started
6/27	15.5	5.08	9,800	.....	..	..	..	..	..	..	..	13.6	
6/28	....	....	.....	.....	..	..	..	..	..	..	..	10.2	
6/29	11.0	4.04	15,450	.....	78	64	14	14	6	..	1	8.8	
6/30	14.0	4.58	15,000	.....	73	51	22	12	12	2	1	6.9	
7/ 1	13.0	4.40	12,300	.....	75	62	13	22	1	..	2	8.0	
7/ 2	....	....	.....	.....	..	..	..	..	..	..	..	5.6	
7/ 4	....	....	.....	.....	..	..	..	..	..	..	..	....	Cyanosis, dyspnea
7/ 5	11.5	4.01	13,450	.....	77	52	25	16	7	..	..	4.2	
7/ 6	....	....	.....	.....	..	..	..	..	..	..	..	....	Nausea, vomiting
7/ 7	10.8	3.39	16,050	.....	87	63	24	9	4	..	..	0.8	
7/ 8	10.8	3.98	14,050	.....	87	59	28	8	4	..	1	2.8	
7/ 9	11.0	3.57	12,550	.....	84	72	12	10	4	..	2	5.0	Macular rash of chest and abdomen
7/11	9.5	2.97	8,500	.....	..	..	..	..	..	..	..	4.8	Sulfanilamide discontinued
7/12	10.0	3.10	5,300	.....	56	44	12	38	4	..	2	...	Sternal marrow; polymorphonuclears, 0.2%
7/13	9.5	3.03	1,900	.....	12	10	2	82	4	..	2	...	Jaundice; blood transfusion started
7/14	8.0	2.81	50	548,500	1	..	..	97	..	1	1	0.0	
7/15	8.5	3.04	700	.....	4	3	1	91	..	4	1	...	
7/16	8.5	2.809	450	.....	..	..	..	99	..	1	..	...	Ulcer of tongue
7/17	8.3	2.98	850	.....	5	3	2	95	..	..	..	...	
7/18	...	....	...	.....	..	..	..	..	..	..	..	...	Patient died

ication could not be administered by mouth because of nausea and vomiting. The sulfanilamide level had now fallen to 0.8 mg. per hundred cubic centimeters. Sulfanilamide 30 grains (2 Gm.) in 300 cc. of water subcutaneously twice a day was prescribed.

July 8 another roentgenogram of the chest, made on a portable machine, showed no consolidation. July 9, reexamination of the sputum revealed group IV pneumococci. A faint erythematous macular rash was seen over the upper abdominal and chest regions. The sulfanilamide level of the blood on this date was 4.8 mg. per hundred cubic centimeters. Hemoglobin was 11 Gm., erythrocytes numbered 3,570,000 and leukocytes 13,550, with polymorphonuclears 84 per cent, lymphocytes 10 per cent, monocytes 4 per cent and eosinophils 2 per cent.

Sulfanilamide was discontinued July 11 because there was no improvement in the patient's condition and toxicity caused by the drug was feared. At this time the hemoglobin content had fallen to 9.5 Gm., the erythrocytes to 2,970,000, leukocytes to 8,500 and the sulfanilamide level to 4.8 mg. per hundred cubic centimeters of blood. The next day the temperature, pulse and respiration rate dropped to 99, 96 and 30 respectively, although there was no appreciable change in the clinical appearance of the patient. That day, July 12, the blood picture first revealed a neutropenia with hemoglobin of 10 Gm., erythrocytes 3,100,000, leukocytes, 5,300, polymorphonuclears 56 per cent, lymphocytes 38 per cent, monocytes 4 per cent and eosinophils 2 per cent. July 13, however, there was another sharp rise in temperature to 104 and a mild jaundice of the scleras and skin developed. The blood picture showed leukocytes 1,900, polymorphonuclears 12 per cent, lymphocytes 82 per cent (some young lymphocytes

Comment.—The patient had had 64 Gm. of sulfanilamide in fifteen days. Cyanosis and dyspnea were noted eight days, nausea and vomiting were seen ten days and an erythematous, macular rash was seen thirteen days after initiation of therapy.

TABLE 2.—*Summary of Reported Fatal Cases of Granulocytopenia Following Sulfanilamide*

	Amount of Drug, Gm.	Number of Days	Death (Days After Discontinued)
Borst [2]	50	28	5
Young [3]	54	18	5
Model [4]	54	18	3
Plumer [5]	45.3	35	5
Berg and Holtzman [6]	38	33	3
Schwartz, Garvin and Koletsky [8]	56.6	21	5
O'Connell [9]	24.3*	7	3
Mitchell and Trachsler [10]	?	?	?
Bernstein [7]	34.8	26	3
Authors' case	64	15	7
Average	50	27	4.8

* Believed to have taken an additional unknown amount of sulfanilamide over three more weeks.

Jaundice was present two days after sulfanilamide had been stopped. Although the hemoglobin and red blood cell count showed a progressive fall from early in the course of the acute illness, the leukopenia and neutropenia were not manifest until the day after the drug was discontinued. The patient died seven days after the withdrawal of the drug. In an attempt to

stimulate hemopoiesis 110 cc. of pentnucleotide, 4 cc. of liver extract and five transfusions, totaling 1,550 cc. of citrated whole blood were administered in four days. The sulfanilamide used was prontylin (Winthrop) by mouth and sulfanilamide (Abbott) subcutaneously. During his hospital stay the only other drugs administered were codeine sulfate, phenobarbital, pitressin and acetylsalicylic acid.

Necropsy.—Postmortem examination was performed four hours after death. The positive observations are presented

Fig. 1.—Superficial mucosal ulceration of tongue. Note colonies of bacteria in submucosal and muscular layers, scattered round cell infiltration and absence of polymorphonuclear leukocytes. Slightly reduced from a photomicrograph with a magnification of 50 diameters.

here. In the right pleural cavity there was 75 cc. of clear straw-colored fluid. The upper and middle lobes of the right lung were a dark purple and edematous. The lower 4 cm. of the right lower lobe showed a sharply delimited, slightly raised area of consolidation covered by a fibrinous pleural exudate. The consolidation measured 6 by 4 by 4 cm. On section this area was seen to be a reddish gray. A firm grayish-white, partially organized thrombus was found in the lower branch of the right pulmonary artery. The thrombus was intimately adherent to the wall of the vessel. Microscopic examination showed extensive edema and congestion, with large areas of necrosis containing many colonies of bacteria but without associated inflammatory cell reaction. The few cells found were of the mononuclear (histiocytic) type.

The tongue showed a shallow ulceration with a dirty gray base which extended from the tip to the midportion of the organ. Microscopically a superficial loss of epithelium was seen. Many colonies of bacteria were present in the submucosal and muscular layers of this section. The inflammatory reaction was mild, characterized by a scattered infiltration of lymphocytes, plasma cells and histiocytes. Edema and congestion also were seen.

The cardiac portion of the esophagus presented several shallow ulcerations of the mucosa and scattered small yellow plaques. The microscopic picture was that of patchy necrosis and hemorrhagic extravasation in the mucosa. The remainder of the section showed edema and congestion with a mild infiltration of mononuclear cells.

The liver was larger and heavier than usual and weighed 2,400 Gm. The organ was a diffuse dark red and was engorged with blood. Sections showed hepatic congestion and edema with a moderate perilobular lymphocytic infiltration. A good deal of iron-containing pigment was demonstrated by the prussian blue stain. The iron pigment was present in clumps and in scattered Kupffer cells.

The spleen was larger and heavier than normal and weighed 250 Gm. This organ was also dark red, cut with increased resistance to reveal a severely congested tissue. Microscopic sections showed hyperemia and quantities of iron-bearing pigment.

The kidneys were large and congested, with depressed scarred areas beneath their capsules. Microscopic examination revealed scattered hyalinized glomeruli, cloudy swelling of the tubules, aggregates of lymphocytes in the interstitial tissue, sclerosis with narrowing of the larger arteries and engorgement of all the blood vessels.

The bone marrow at the ends of the humerus and femur as well as of the vertebrae appeared yellow and fatty. Microscopic examination of the bone marrow from the end of the femur showed almost no cellular elements. The bone marrow from the end of the humerus showed moderate cellularity, with a differential count of primitive cells 4 per cent, blast forms 40 per cent, myelocytes 6 per cent, lymphocytes and plasma cells 30 per cent, megaloblasts 5 per cent and normoblasts 15 per cent.

The gross pathologic diagnoses were embolism of the lower branch of the right pulmonary artery with infarction in the right lower lobe; acute hyperemia of the liver, spleen, kidneys and stomach; mucosal ulcerations of the tongue and esophagus; arterial nephrosclerosis; chronic cholecystitis. The microscopic diagnoses were pulmonary infarction, necrotizing bronchopneumonia, mucosal ulceration of the tongue and the esophagus with general edema and congestion; edema and congestion of the liver and walls of the stomach; hemosiderosis of the liver and spleen; arterial nephrosclerosis, chronic pyelonephritis, benign corticorenal adenoma; myeloblastic arrest of the cells of the bone marrow and granulocytopenia.

REVIEW OF REPORTED CASES

A review of fatal granulocytopenia included nine cases reported in American and English journals.

In Borst's [2] case more than 50 Gm. of prontosil (the disodium salt of 4-sulfamido-phenyl-2′-azo-7′ acetyl-amino-1′-hydroxynaphthalene-3,′ 6′ disulfonic acid) in

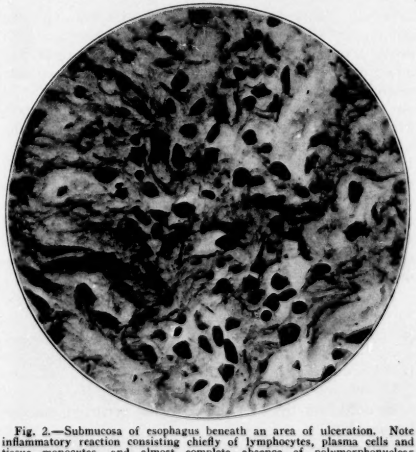

Fig. 2.—Submucosa of esophagus beneath an area of ulceration. Note inflammatory reaction consisting chiefly of lymphocytes, plasma cells and tissue monocytes, and almost complete absence of polymorphonuclear leukocytes. Slightly reduced from a photomicrograph with a magnification of 500 diameters.

twenty-eight days was given to a white woman, aged 61, with Escherichia coli pyelocystitis. The first symptoms of toxicity were those of general discomfort and mild fever. The drug was discontinued the next day. Sore throat was noticed the following day, when the blood count showed leukocytes 1,225, polymorpho-

1. Footnote deleted on proof.
2. Borst, J. G. G.: Lancet **1**: 1519 (June 26) 1937.

nuclear leukocytes 5 per cent, hemoglobin 70 per cent, erythrocytes 3,300,000. The patient died two days after therapy was discontinued, on which day the count was leukocytes 960 and polymorphonuclear leukocytes 1 per cent. Atelectasis of the left lower lobe was the only finding reported from the postmortem examination.

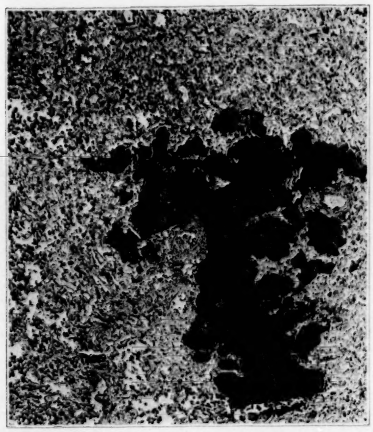

Fig. 3.—Necrotizing pneumonia with large colonies of bacteria, edema, hyperemia and little inflammatory reaction; × 50.

In the Young [3] case 54 Gm. of sulfanilamide was administered in eighteen days to a man aged 53 with acute articular rheumatism. A cutaneous rash was noted during treatment. One day before the drug was discontinued the white cells numbered 7,800 with 73 per cent polymorphonuclear leukocytes. Four days after the sulfanilamide was stopped the white cells numbered 1,800 with no polymorphonuclear cells. Death occurred five days after the cessation of the drug. Postmortem examination revealed a grayish membranous exudate over the pharynx with no polymorphonuclears seen microscopically. The liver weighed 1,555 Gm., the spleen 175 Gm. The bone marrow was aplastic and contained no granulocytes. Lymphocytes, megakaryocytes and nucleated red cells were seen.

In Model's [4] case 54 Gm. of para-aminobenzene sulfonamide (proseptasine May and Baker) was given in eighteen days to a man aged 20 with acute rheumatic fever. Two days after the drug was discontinued the blood count was hemoglobin 45 per cent, erythrocytes 2,900,000 and leukocytes 600; gray spots in the pharynx were noted for the first time. Death occurred the following day.

Plumer [5] presented a case of subacute bacterial endocarditis in a woman aged 54 who during thirty-five days was treated with 45.3 Gm. of sulfanilamide. After this time nausea and vomiting developed and the drug was discontinued. Three days after the sulfanilamide was stopped the erythrocytes numbered 3,580,000, the leukocytes 400 with no polymorphonuclear leukocytes. The following day a gangrenous infection of the mouth and pharynx was noted. The leukocyte count was 1,600. The patient died five days after the drug was discontinued.

In the Berg and Holtzman [6] case 58 Gm. of sulfanilamide in thirty-three days was given to a man aged 22 with acute gonorrhea. Treatment was continued despite numerous toxic reactions. The last blood count recorded hemoglobin 60 per cent, erythrocytes 2,600,000, leukocytes 1,600 with no polymorphonuclear leukocytes.

Bernstein's [7] patient, an infant aged 6 months, had bronchopneumonia, otitis media and erysipelas. She was treated for fourteen days, receiving 9.4 Gm. of sulfanilamide orally and 35 cc. of prontosil intramuscularly. After an interval of thirteen days treatment was resumed over a period of twelve days, the patient receiving 8 Gm. of sulfanilamide orally and 35 cc. of prontosil intramuscularly. Two days after resumption of treatment jaundice developed. Granulocytopenia was first observed three days after the final cessation of therapy.

Schwartz, Koletsky and Garvin [8] reported the case of a man aged 32 who received 56.6 Gm. of sulfanilamide in twenty-one days of treatment for a penile ulcer—a possible chancroid. August 13 a blood count of 3,900 leukocytes and 4,140,000 erythrocytes was noted with no subjective complaints. August 16, the day the drug was stopped, the blood report was leukocytes 2,000 with no polymorphonuclear leukocytes and 3,410,000 erythrocytes, still with no subjective complaints. Typhoid bacilli (20 million) were given the following day to stimulate development of leukocytes. Following the typhoid treatment the temperature rose from normal to 104.9 F. and persisted. Four days after the drug was withdrawn sore throat and difficulty in swallowing were reported. Examination revealed a

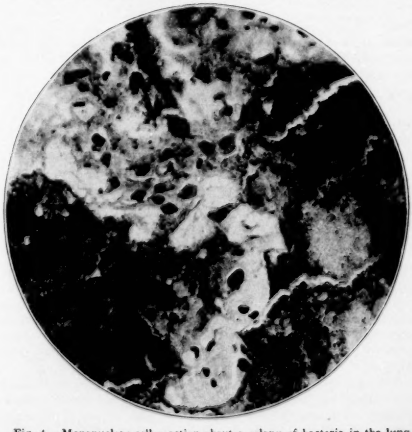

Fig. 4.—Mononuclear cell reaction about a colony of bacteria in the lung. Note virtual absence of polymorphonuclear leukocytes. Slightly reduced from a photomicrograph with a magnification of 500 diameters.

3. Young, C. J.: Brit. M. J. **2**: 105 (July 17) 1937.
4. Model, Alfred: Brit. M. J. **2**: 295 (Aug. 7) 1937.
5. Plumer, H. E.: New England J. Med. **216**: 711 (April 22) 1937.
6. Berg, Samuel, and Holtzman, Michael: Fatal Granulocytopenia Following Sulfanilamide Therapy, J. A. M. A. **110**: 370 (Jan. 29) 1938.
7. Bernstein, S. S.: J. Pediat. **11**: 198 (Aug.) 1937.
8. Schwartz, W. F.; Garvin, C. F., and Koletsky, Simon: Fatal Granulocytopenia from Sulfanilamide, J. A. M. A. **110**: 368 (Jan. 29) 1938.

necrotic ulceration of the mucosa in the tonsillar region. The scleras were icteric and the liver edge was palpable 3 cm. below the costal margin. The patient died five days after sulfanilamide was discontinued.

The postmortem examination revealed hyperemia and edema of the larynx with a lymphocytic infiltration. The lungs, liver and spleen were hyperemic with

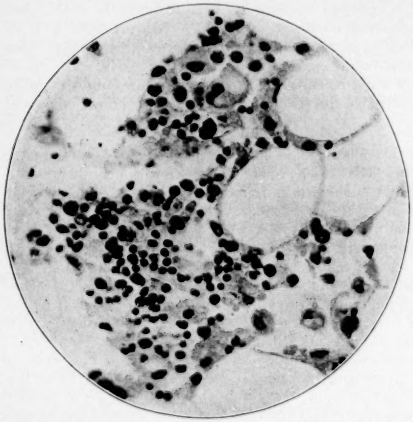

Fig. 5.—Bone marrow of the humerus. In addition to normoblasts there are leukoblasts, myelocytes, lymphocytes and plasma cells but no polymorphonuclear leukocytes. Slightly reduced from a photomicrograph with a magnification of 500 diameters.

large quantities of iron-bearing pigment. The cellular picture of the hemopoietic tissue was within normal limits. The differential count was myeloblasts 55 per cent, lymphocytes 35 per cent (with occasional plasma cells) and nucleated red cells 15 per cent.

O'Connell [9] reported the case of a seaman treated for chronic gonorrhea with 24.3 Gm. of sulfanilamide over a period of seven days. Treatment was discontinued because of "acute catarrhal fever." Three weeks later the patient returned to the hospital with symptoms of granulocytopenia. Death occurred three days after onset of his acute illness. After death a partially filled bottle of sulfanilamide tablets was found among his effects. The changes found at autopsy were reported as agranulocytosis and edema of the glottis.

Mitchell and Trachsler [10] presented a case seen by them in which large doses of sulfanilamide were employed over a long period of time in the treatment of chronic infectious arthritis. A severe anemia, neutropenia and necrotic stomatitis developed and the patient died. The condition found at autopsy was not reported.

COMMENT AND SUMMARY

The pathologic changes in our case agree with those of the few postmortem examinations which have been made. The fundamental picture is that of a toxic granulocytopenia with arrest of the maturation of the blast forms of the myeloid series such as has been reported for other toxic drugs. The jaundice, the quantities of hemosiderin in the liver and spleen as well as the bone marrow count support the impression that the anemia was of a hemolytic nature due to the toxic action of the sulfanilamide. We cannot agree with the opinion of some writers that this action on the bone marrow is due to specific idiosyncrasy. The quantity and the prolonged use of the drug we feel are the significant factors.

In these ten cases of fatal granulocytopenia, the doses of sulfanilamide preparations ranged from 35 to 64 Gm. with an average of 50 Gm. The length of time that the drug was administered ranged from fifteen to thirty days with an average of twenty-seven days of therapy. Thus in all these cases large doses of the drug were administered over long periods of time. It is the impression of clinicians [11] who have had large institutional experience with the drug that the efficacy of sulfanilamide in a given condition should be demonstrable after from four to seven days. If no improvement is noted within that period the continued use of the drug is of doubtful value.

All the reviewed cases except that of Schwartz and his associates [8] showed toxic symptoms during the use of sulfanilamide. Toxic symptoms are very common during this therapy. Certain of these reactions, however, should be considered as warning signals, i. e., cutaneous eruptions, hyperpyrexia, jaundice, gradual fall in red blood cells and hemoglobin and an abrupt rise or fall in white blood cells. As has been suggested by Bannick and his associates,[12] if mild to moderate toxic symptoms appear decrease in dosage or cessation of the drug for a few days is advisable. If symptoms persist

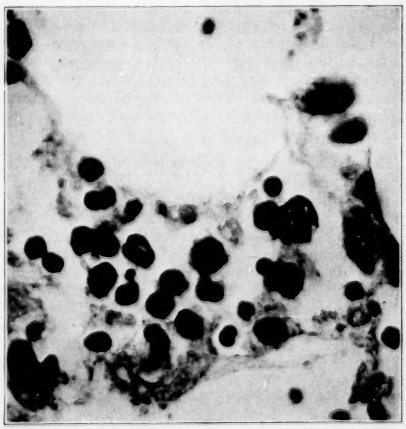

Fig. 6.—Bone marrow of the humerus. Same as figure 5, × 1,000.

or recur after decrease or on resumption of the drug, permanent discontinuance of the therapy is indicated.

A close check on the blood picture was not made in most of these fatalities. Blood counts were not done frequently. Three cases were not brought under the care of the reporting authors until the granulocytopenic

9. O'Connell, J. T.: U. S. Nav. M. Bull. **36**: 61 (Jan.) 1938.
10. Mitchell, A. G., and Trachsler, W. H.: J. Pediat. **11**: 183 (Aug.) 1937.
11. Price, A. E., and Myers, G. B.: Unpublished data.
12. Bannick, E. G.; Brown, A. E., and Foster, F. P.: Therapeutic Effectiveness and Toxicity of Sulfanilamide, J. A. M. A. **111**: 770 (Aug. 27) 1938.

state had been reached. The patients had been treated on the outside or had practiced self medication. Careful daily blood studies are indicated when sulfanilamide is used for any length of time.

Granulocytopenia was not manifest in six of the reported cases until from one to four days after the drug was stopped. In Young's case, in which blood counts were taken frequently, one day before the drug was discontinued the white cells numbered 7,800 with 73 per cent polymorphonuclears. In our case, two days before sulfanilamide was stopped leukocytes numbered 12,550 with 84 per cent polymorphonuclears; the day of discontinuance the white cell count was 8,500. Blood studies for a few days after cessation of therapy would seem to be a valuable procedure.

Sulfanilamide is an exceedingly valuable drug which is being widely used, yet, there have been relatively few fatalities reported. The drug should be administered only under careful supervision. The use of sulfanilamide in conditions in which its value is not established should be reserved for cases under institutional direction. Legislation is necessary to prevent dispensing the drug without prescription.

STRONGYLOIDIASIS

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The title of this paper describes an abnormal condition resulting from a parasitic invasion of the human body. It has been sixty-two years since Normand [1] chronicled his observations of the condition in the French soldiers returning from Cochin China (1876), but little has appeared in medical literature since. Bavay in the same year observed a large number of infested workers in the St. Gothard tunnel and attempted some description of the parasite. In the United States the pioneer observer was Strong.

PATHOGENICITY

Debate continues to rage around the query "Are the parasites pathogenic?" So far as the animal experimental work may aid conclusion, it appears that Sandground [2] has demonstrated that they can cause symptoms. The failure to convict Strongyloides in the case of Cochin China diarrhea has perhaps been a factor in the rather general thought that the parasite causes no symptoms. Yet cases are found in the literature in which the symptoms are as definite as may be observed with infestation by other members of the nematode family. Likewise, reports of relief from such symptoms after the eradication of the larvae from the stools would appear as legitimate evidence of pathogenicity. Eosinophilia appears to be present in a percentage comparable to that in infestations by other nematodes. This argues an allergic response. This allergy shows some peculiarities. Sandground showed that the host organism produces no antigen against the filariform larvae themselves except when they undergo certain functional changes, such as maturation. When Rhabditis larvae are used as antigen, complement fixation is more uniform.

Pathogenicity of the parasite is often dismissed with the statement that "it usually produces little harm." This is in contrast to the opinion of Barlow, who classified the stages of strongyloidiasis as (1) a period of pruriginous cutaneous lesions, the result of larval invasion, (2) a latent period, (3) a period characterized by diarrhea and (4) a period of neurasthenia.

Ginsburg's [3] patient had been ill but three weeks when admitted to the hospital and died one month later. While necropsy was not performed, no other cause was found clinically to explain the death. In one of the most recent articles on the parasite Hinman [4] called inevitable the conclusion that the parasite is pathogenic.

DISTRIBUTION

De Rivas [5] said that the parasite may be found in the "territories where the hookworm is prevalent." Since hookworm is found in 33 per cent of the population of eleven Southern states, according to Rhoads,[6] one may well wonder why strongyloidiasis is not more frequently reported.

De Rivas's observation does not parallel that of Keller,[7] who studied fifty-two counties in Tennessee and found hookworm in forty-three, with an incidence of 7.4 per cent. Several other intestinal parasites were noted, but not Strongyloides. Cadham [8] reported a case from Winnipeg and commented on the rarity of this parasite in Canada. It was estimated by Faust that 6 per cent of the clinic population of New Orleans was infested. Thonnard-Neumann [9] ranked the parasite in order of its frequency with other parasites as follows: Endamoeba twenty-eight cases, Uncinaria twenty-three, Trichocephalus twenty-two, Lamblia twenty-one, Strongyloides seven and Ascaris four. Eusterman and Balfour [10] expressed the belief that infestation is not as rare as clinical reports would indicate and is widespread in the Southern states. Ginsburg reported the case of a woman who was born and had lived all her life in western Pennsylvania. Manson-Bahr [11] expressed the opinion that the parasite has a worldwide distribution. Faust reported a 4 per cent incidence among the inpatient and outpatient hospital population in New Orleans; the incidence among the city population was stated to be much less, but no estimate was made. Faust and his associates [12] found a 4.6 per cent incidence in Puerto Rico in 1934 and expressed the belief that the distribution of Strongyloides approximated that of hookworm. Byrd [13] reported 0.37 per cent infestation in Athens, Ga., in 1936. Headlee and

Read before the Section on Gastro-Enterology and Proctology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

1. Normand, A.: Sur la maladie dite diarrhea de Cochin-Chine, Compt. rend. Acad. d. sc. **5**: 316, 1876.
2. Sandground, J. H.: The Role of Strongyloides Stertorcalis in the Causation of Diarrhea, Am. J. Trop. Med. **6**: 421 (Nov.) 1926.
3. Ginsburg, Louis: Strongyloides Intestinalis Infestation, J. A. M. A. **75**: 1137 (Oct. 23) 1920.
4. Hinman, E. H.: Clinical Aspects of Strongyloides Stercoralis Infection, Rev. Gastroenterol. **5**: 24 (March) 1938.
5. De Rivas, Damaso: Parasites, in Piersol, G. M.; Bortz, E. L., and others: Cyclopedia of Medicine, Philadelphia, F. A. Davis Company, 1934, vol. 9, p. 634.
6. Rhoads, C. P.: Hook Worm Disease, in Cyclopedia of Medicine, vol. 9, p. 614.
7. Kellar, A. E.: Field Studies of Human Intestinal Parasites in Tennessee, South. M. J. **24**: 336 (April) 1931.
8. Cadham, Fred T.: Infestation with Strongyloides Stercoralis Associated with Severe Symptoms, Canad. M. A. J. **29**: 18 (July) 1933.
9. Thonnard-Neumann, Ernst: Treatment with Di-Hydranol of Intestinal Protozoal and Helminthic Infections in Man: A Preliminary Report, Twentieth Annual Report, 122, 1931, United Fruit Company, Medical Department, 1931, p. 122.
10. Eusterman, G. R., and Balfour, D. C.: The Stomach and Duodenum, Philadelphia, W. B. Saunders Company, 1935, p. 425.
11. Manson-Bahr, P. H.: Manson's Tropical Diseases, ed. 10, New York, William Wood & Co., 1936.
12. Faust, E. C.; Hoffman, W. A.; Jones, C. A., and Janer, J. L.: A Survey of Intestinal Parasites in Endemic Schistosomiasis Areas in Puerto Rico, Puerto Rico, J. Pub. Health & Trop. Med. **9**: 447 (June) 1934.
13. Byrd, E. E.: On the Incidence of Intestinal Parasites in 537 Individuals on the Relief Rolls in the City of Athens, Georgia, and Vicinity, Am. J. Trop. Med. **16**: 39 (Jan.) 1936.

Cable [14] examined 514 students of the junior high school and of Berea College, Berea, Ky., in 1936 and found infestation with helminths in 31.9 per cent. Strongyloides had a percentage incidence of 2.7. The students came from fifteen states and a few from foreign countries. Forty-eight of 120 counties of Kentucky were represented. Hinman [15] found eighty-five cases of infestation in Louisiana in 1937. No extensive study of cross sections of the population of the Northern states has been made, but it is not probable that the incidence is as high as in the Southern states. Cordi and Otto [16] attempted to explain this difference on the basis of a poor adaptability of both eggs and larvae to changes in temperature.

LIFE HISTORY OF THE PARASITE

The usual story is that Strongyloides stercoralis invades the human being much after the manner of the hookworm. 1. The skin or mucosa is penetrated by the filariform larvae, which pass into the venous circulation through the heart and enter the alveoli of the lungs, whence they migrate to the epiglottis and on to the intestinal tract. 2. They may enter the digestive tract direct and attach themselves to the mucosa of the duodenum or jejunum or enter the crypts and develop into adult worms. They exist as male and female.

The most common method of development, however, is the hatching of the eggs in the intestine and their passage from the canal as rhabditiform larvae, after which they enter the filariform, infective stage. On the other hand, the larvae may become transformed into male and female worms and the eggs from these females hatch as rhabditiform larvae, which molt after a few days and become the infective filariform larvae.

The life history of this parasite then offers two phases of development, (*a*) a parasitic or intestinal form and (*b*) a free-living or fecal form. The first is represented by the female worm only, which is one-twelfth inch long and reproduces parthenogenetically. The worm is translucent and hence may easily be overlooked when one is examining the intestine at autopsy with a hand lens. It is most easily found by scraping the mucosa and studying the material under the microscope with a two-thirds inch lens. Only actively motile embryos are found in the feces. Eggs are found only when the stool is obtained by catharsis. Keeping this fact in mind helps to differentiate hookworm from Strongyloides eggs. Stitt [17] dogmatically says: "In fresh feces one finds hookworm eggs and Strongyloides embryos." When kept at a high temperature the embryos develop in the free-living or fecal form. The parasites are now found living as male and female and reproduce the larvae, which are capable of starting a parasitic generation in the original host or a new one by ingestion. Failing to reach the intestinal canal of some mammal, they die.

The adult worms are found in greatest numbers in the duodenum, and the number lessens in succeeding divisions of the small bowel; they are rarely found in the large bowel. The head of the female pushes into the crypts of the glands of Lieberkühn; eggs are found there as well as between epithelial cells and even as deep as the basement membrane. When the eggs hatch, the larvae may encyst and be found in intraglandular lymphoid tissue, even as far as the lymphatic follicles of the submucous coat. Adult worms have been found in the stomach at autopsy, and Ophüls [18] observed ova and rhabditiform larvae there as well. Eusterman and Balfour say that when infestation is heavy larvae may be found in large numbers.

CLINICAL PICTURE

Since the parasite has a bizarre career in the human body, making its domicile with equal adaptability in the stomach, duodenum, biliary passages, pancreatic ducts, ileum, jejunum, cecum, colon, cutaneous blood vessels, lungs and trachea, a description of a clinical syndrome becomes difficult. When the entry has been through the skin a reactionary erythema begins within twenty-four hours at the site of entrance. This increases in degree for another twenty-four or forty-eight hours and is made more annoying by itching. These symptoms appear to be much aggravated in sensitized persons. Varying degrees of irritation, even inflammation, in lung tissues appear, while a low grade infestation may cause no clinical phenomena. In the digestive tract, whether reached by the skin-lung route or by direct conveyance to the stomach and bowel, the clinical picture varies from no disturbance or a negligible one to severe, even fatal diarrhea. Wagner [19] reported a case in which bloody diarrhea was present and superficial ulcers were seen proctoscopically some 6 inches above the anal sphincter. Colitis may be caused by the penetration of the colonic mucosa by the filariform parasites.

In de Langen's [20] group leukocytosis, a low hemoglobin content, epigastric pain, intermittent diarrhea, low grade pyrexia and bronchopneumonia were listed. Faust's group showed a much less severe syndrome; alternating diarrhea and constipation appeared as the most common symptoms.

Urticaria is rather frequently noted in strongyloidiasis. Whenever it occurs it is thought to be the result of direct irritation by the larvae as they penetrate the skin. In the case reported by Cadham intermittent diarrhea, recurring urticaria and neurasthenia with edema, emaciation and progressive anemia were interesting features.

Obstructive jaundice resulting from Strongyloides larvae was reported by Nisbet.[21] The larvae were found in the feces and also recovered by transduodenal drainage. A convalescent period of three months was recorded. In the chronic states emaciation and anemia supervene, and edema may follow in their wake. Death may ensue from a massive infestation. As long ago as 1876 Normand reported five deaths in Cochin China. Ophüls observed fatalities in temperate zones. Ginsburg has reported similar observations.

Hinman found abdominal pain to be the chief complaint in a group of eighty-five cases reported in 1937; it varied in intensity, location and character. Abdominal tenderness alone was described in twenty-nine and was localized in the right lower quadrant in eight; in only three was it diffuse. A tentative diagnosis of appendi-

14. Headlee, W. H., and Cable, R. M.: Studies of Intestinal Parasite Infections of Students of Berea College, Kentucky, J. Parasitol. **22**: 530 (Dec.) 1936.

15. Hinman, E. H.: A Study of Eighty-Five Cases of Strongyloides Stercoralis Infection with Special Reference to Abdominal Pain, Tr. Roy. Soc. Trop. Med. & Hyg. **30**: 531 (March) 1937.

16. Cordi, J. M., and Otto, G. F.: The Effect of Various Temperatures on the Eggs and Larvae of Strongyloides, Am. J. Hyg. **19**: 103 (Jan.) 1934.

17. Stitt, E. R.: Practical Bacteriology, Blood Work and Animal Parasitology, ed. 8, Philadelphia P. Blakiston's Son & Co., 1927, p. 477.

18. Ophüls, W.: A Fatal Case of Strongyloidosis in Man, Arch. Path. **8**: 1 (July) 1929.

19. Wagner, Jerome: A Case of Bloody Diarrhoea Due to Strongyloides Intestinalis, Internat. J. Surg. **34**: 398 (Nov.) 1921.

20. de Langen, C. D.: Anguillulosis and the Syndrome of the "Idiopathic Hypereosinophilia," Mededeel. v. d. dienst. d. volksgezondh. in Nederl.-Indie **27**: 515, 1928.

21. Nisbet, D. H.: Obstructive Jaundice Due to Strongyloid Larvae, South. Med. & Surg. **94**: 785 (Dec.) 1932.

citis was made in five. In twenty-six diarrhea was noted; the stools were bloody in fourteen. The average loss of weight was 14½ pounds (6.7 Kg.). In only nineteen cases was the finding of Strongyloides incidental to admission to the hospital.

The diagnosis of strongyloidiasis, however, must be made through laboratory studies, interesting as clinical phenomena may be. Reasoning from analogy, one would expect an increase in the eosinophils, but it is interesting to note that Hensen [22] reported a series of cases of intestinal infestation of several varieties, but none of strongyloidiasis, in which there was no eosinophilia. By the same yardstick one is prepared for an absence of eosinophils in strongyloidiasis. Wagner [23] expressed the belief that a value of 50 per cent is not uncommon. Hensen reported a value of 82 per cent in another series. In Levin's [24] group of eleven cases the highest eosinophil count was thirteen, and in five the count was five or less. Hinman expressed the opinion that eosinophilia is more frequent with infestations by Strongyloides than with those by other helminths, except Trichinella. Both of these invade tissues rather constantly, and hence a more significant eosinophilia is expected.

Perhaps the question was best summed up by Faust [25] when he stated that there is marked eosinophilia as well as leukocytosis during the period of invasion, incubation and early oviposition, and that both decrease as the infestation becomes chronic.

Complement fixation tests have been studied by Cosack and Schmidt [26] and stated to be of little value. Cutaneous sensitization tests may be suggestive in a small percentage of cases. Study of feces is the easiest approach and when larvae are demonstrated suffices. The larvae are very motile. Care must be exercised in studying specimens, as vegetable fibers may be mistaken unless motion is observed. When the stool is formed the larvae will best be found by making a dent in the fecal mass, filling this with water and keeping it in an incubator for twenty-four hours. The larvae gravitate into this pool and are easily found under the microscope with a 16 mm. objective (Kolmer and Boerner [27]).

Hookworm infestation is most likely to be confused with strongyloidiasis. The embryos of hookworm are usually found in the unhatched eggs. The parasite is easily found in the feces, the contrary being true of Strongyloides. But when one reflects that in the majority of cases the stools will be normal unless obtained by purgation, some other procedures must usually be followed. As it is known that the duodenum harbors the major number of the parasites, a simpler and surer way is a study of duodenal fluid obtained by transduodenal drainage. In every case that I have studied parasites have been found in the duodenum. This method should be followed in every case in which parasitic infestation is suspected. It serves as usefully in evaluating the efficacy of therapy. Relief should not be assumed from study of the feces alone. Until both feces and duodenal contents are normal, conclusion of eradication is unwarranted. In this detail it is well to remember the injunction of Cordi and Otto [16] that intestinal specimens should not be stored in an ice box for as long as ten hours before examination for Strongyloides.

22. Hensen, N.: Deutsche med. Wchnschr. **49:** 83, 1923 (trans.).
23. Wagner, E. A.: Strongyloides Stercoralis, Ohio State M. J. **32:** 826 (Sept.) 1936.
24. Levin, A. L.: The Problem of Eradication of Strongyloides Intestinalis, Am. J. Trop. Med. **10:** 353 (Sept.) 1930.
25. Faust, E. C.: Human Strongyloidiasis in Panama, Am. J. Hyg. **14:** 203 (July) 1931.
26. Cosack, Gert, and Schmidt, Gertrude: Ueber Anguillulosis (Strongyloides Stercoralis), Jahrb. f. Kinderh. **143:** 208 (Oct.) 1934.
27. Kolmer, John A., and Boerner, Fred: Approved Laboratory Technic, New York, D. Appleton-Century Company, Inc., 1931, p. 220.

TREATMENT

The lack of appreciation of the pathogenic nature of strongyloidiasis exerted of course an influence on the interest in its therapeusis. Then, too, additional factors served to perpetuate a desultory concern with remedial measures: 1. Since the agent was a worm and the pharmacologies of the day listed a goodly number of vermifuges and vermicides said to be worth while, why search for a new one? 2. Though its habitat came to be known rather early, disappearance of ova and larvae from the feces continued to be regarded as a measure of the efficiency of the drug used.

Thymol came to be used for this purpose, and in a single case reported in 1921 Wagner [19] described rather spectacular results. So enthusiastic was he that he described in considerable detail his method. He starved the patient for twenty-four hours and gave 30 grains (2 Gm.) of thymol at the next bedtime; 8 ounces (236 cc.) of magnesium citrate was given the following morning, and two hours later a second dose of thymol was administered. Food was permitted the following day. This procedure was repeated twice on the third succeeding days. Administration of a total of 120 grains (8 Gm.) thus constituted the course of treatment, and the diarrhea was reported as having ceased in three days after the second course of treatment. Twelve years later Cadham,[8] impressed by the comparatively few reports in the literature of treatment with thymol, tried it on his patient and added his to the list of successes.

Thonnard-Neumann [9] reported the use of dihydranol (heptylresorcinol) in a series of thirty-one cases of helminthiasis, seventeen of infestation by Strongyloides; in all relief followed. The drug was administered in increasing doses, beginning with 0.9 Gm. daily, increasing to 1.8 Gm. by the third day of treatment and continuing at this level for a varying period, apparently determined by results. Each daily dose was dissolved in olive oil, divided into three capsules and given one after each meal. The author concluded that the drug has a negligible toxicity, and no so-called cumulative effects were noted up to a total dose of 17.5 Gm. in a single series.

Gentian violet as a bactericidal agent was emphasized by Churchman in 1912. Its role as a helminthicidal agent was stressed by Faust [28] in 1929. His first observations were with the Chinese liver fluke, and the drug was given both orally and intravenously. He and his associates found that the drug was tolerated up to 35 mg. per kilogram of body weight by both human beings and experimental animals. In 1930 he treated a series of patients under 10 years of age at Tulane University, the drug being given orally in doses of 0.5 Gm. in enteric-coated tablets three times daily. The parasites were eradicated in the series with one exception and remained absent for three months. In 1932 [29] he recommended a dose of 0.03 Gm. (one-half grain) three times daily for ten doses. With a knowledge of some 200 patients who were treated with gentian violet, he had examined forty-seven after treatment and found all but two free from parasites. Only four had needed two courses of treatment. In a paper presented in 1937

28. Faust, E. C., cited in Gentian Violet Therapy for Strongyloides Infection, editorial, Internat. M. Digest. **17:** 57 (July) 1930.
29. Faust, E. C.: The Symptomatology, Diagnosis and Treatment of Strongyloides Infection, J. A. M. A. **98:** 2276 (June 25) 1932.

he [30] listed as the most important chemotherapeutic agents for removing intestinal nematodes: thymol, betanaphthol, oil of chenopodium, carbon tetrachloride, tetrachlorethylene, santonin, hexylresorcinol and gentian violet medicinal. Of this group of anthelmintics admitted to the nobility, he classed gentian violet as a specific. He recommended that it be given in an enteric-coated pill in 0.06 Gm. doses three times daily before meals for sixteen and two-thirds days. The implied virtue of the odd two thirds of a day remained unexplained. After stating that the drug is the only one found to be specific, he modestly concluded that it "frequently eradicates the organism." He stated that no satisfactory method of treating pulmonary strongyloidiasis had been devised.

In 1928 de Langen [20] had tried the drug in treating Strongyloides infestation in a dose of one-sixth to one-half grain (0.01 to 0.03 Gm.) three or four times dailv. The symptoms and eosinophilia promptly disappeared, but no mention was made in the translation concerning the disappearance of parasites from the stool.

Santonin, oil of chenopodium, glycerin and felicis maris were all used in turn, with failure, by Kwa Tjaon Sioe.[31] Even a reduction in number of the larvae in the feces was not observed. Sioe observed that these drugs, together with emetine, antimony and potassium tartrate, methylene blue, eosin and gentian violet, did not rapidly kill larvae in cover slip specimens. He gave gentian violet orally and reported success. In his summary he wrote "The action of gentian violet is probably direct on the worms and in vitro it has not more effect than other drugs against the larvae." One finds it difficult to understand how a clinician can harmonize similar observations.

Cosack and Schmidt [26] reported a series of nine cases in which thymol, picric acid and oil of chenopodium were used with failure. Gentian violet was credited with favorable results in five of these. On analysis, however, the term favorable loses significance, as they said "Practically all the specimens were free from larvae" and again that "larvae were present in small numbers."

One may feel justified in concluding that unless a drug frees the canal of adult parasites, ova and larvae, it scarcely merits the confidence implied by the term favorable.

There appears to be no especial contraindication to the use of gentian violet. Nausea and vomiting are rather rare. Violet discoloration of the urine is still more rarely reported. It is claimed that the adult parasitic worm is very susceptible to its toxic effects, looses its attachment to the mucosa and passes in the feces. Singularly, the eggs and young larvae are more resistant. Yet more singularly, it appears that small amounts of the dye modify the indirect type of the parasite into the direct type, which may be said to minimize materially the likelihood of infestation before the parasites are actually killed. The dye stains the mucosa of the intestine a brilliant hue; this is thought to be a vital cytoplasmic reaction.

In 1926 De Rivas [32] described an intra-intestinal thermal method of ridding the intestine of parasites. The method consisted of flushing the bowel with a 30 per cent solution of magnesium sulfate introduced through an ordinary duodenal tube; this was followed by the introduction of 500 cc. of saline solution at a temperature of 46 C. and in ten minutes by a second injection of magnesium sulfate solution. This procedure was to be repeated twice. The rationale of the procedure rested on the fact that intestinal parasites detach themselves from the intestinal wall and frequently are killed by an exposure of from five to ten minutes to a temperature of from 45 to 47 C. (113 to 116.6 F.). De Rivas [5] later described a modification of the method, in which he added an equal amount of glycerin to the preliminary sulfate solution. The added feature of dehydration was claimed to kill the parasites in a shorter period (from two to ten minutes).

Chopra and Chandler [33] said that no treatment known can be relied on for the relief of Strongyloides infestation. Levin [24] spoke of Strongyloides as deserving special mention because it had successfully eluded efforts at eradication. He expressed no doubt as to the pathogenicity of certain members of the family and stated that the digestive tract is more often the avenue of entrance than the skin. I did not read Levin's paper until some three months ago, during the preparation of this paper, and I was surprised to learn that he had found that the larvae can be killed almost instantly in vitro by "95 per cent alcohol, kerosene, glycerin and Gram's iodine solution." However, after trying kerosene and other agents he concluded that "no form of treatment has any permanent value."

Kudicke [34] tested a large number of dyes with a view to determining their chemical and pharmacologic effects on various parasites, including the larvae of Strongyloides. The concentrations necessary to produce toxic effects on the parasites precluded his carrying the tests into the field of observation on animals and human beings.

With such of the aforementioned information as was available up to 1936, the series of cases on which this report is based came under observation. Nine patients have been treated by the method to be described. Since there were no features of especial interest other than the treatment, only one case, the first of the series, will be detailed. Some patients responded promptly, with no recurrence, a result not obtained in the case reported.

The technic developed consisted in the following details: A saline purgative was administered one hour before supper. This was expected to act before the patient's bedtime. Breakfast was withheld the following morning. A transduodenal tube equipped with a Lyon metal bulb was introduced, the stomach irrigated and the tube allowed to pass into the duodenum. The duodenal contents were aspirated for the twofold purpose of securing a specimen for laboratory examination for parasites and to remove contents, thus lessening the dilution of the drug to be introduced into the bowel.

Compound solution of iodine was then introduced into the duodenum and the tube withdrawn. The dose finally fixed was 60 minims (4 cc.) and was given on alternate days until neither the duodenal contents nor the feces showed ova, parasites or larvae. After two weeks the duodenal contents and feces were examined. If the results were negative, the patient was instructed to return in one month for another laboratory study.

The riddance of infestation by the drug given by mouth is believed possible, but the results would surely

30. Faust, E. C.: The Use of Anthelmintics, J. A. M. A. **108:** 386 (Jan. 30) 1937.
31. Sioe, Kwa Tjaon: Strongyloidosis and Its Treatment with Gentian Violet, Far East. A. Trop. Med., Tr. Seventh Cong. **3:** 200, 1930.
32. De Rivas, Damaso: Treatment of Intestinal Parasites by Intra-intestinal Thermal Method, Am. J. Trop. Med. **6:** 47 (Jan.) 1926.
33. Chopra, R. N., and Chandler, A. C.: Diuresis, Anthelmintics and Their Uses, Baltimore, Williams & Wilkins Company, 1928, p. 225.
34. Kudicke, R.: New Methods of Investigation and Trial of Anthelmintics, Experimental Cysticercus and Strongyloides Larvae; abstr. Trop. Dis. Bull. **23:** 242, 1925.

be more slowly secured. The transduodenal method is carried out with too little inconvenience to the patient or consumption of time for the physician to persuade one to trade a reasonably certain method for a doubtful one.

In no case has freedom from worms been recorded on the evidence of normal stools alone; it is insisted that examination of the duodenal fluid must repeatedly show negative results. It is believed that at least some of the cases reported in the literature as instances of riddance of worms would not have been so classed had duodenal drainage been done.

MOP-UP CAMPAIGN

My experience convinces me that riddance of infestation is not assured unless a thorough, systematic cleaning-up program is instituted. The carpets and rugs must be either dry cleaned or exposed to the sun's rays for several days. Wearing apparel not damaged by heat should be boiled; other garments should be dry cleaned. Floors should be scrubbed with soap and hot water. The floors of cellars and outbuildings, if earthen, should be covered with lime; if wood, they should be scrubbed with soap and water. Household pets, dogs and cats, should be either killed or treated. Examination of the water supply has shown no ova in my experience. Examination of every member of the family should be searchingly done. It does not seem reasonable to conclude that the family will escape after one member becomes infested.

Results of Gastric Analysis in a Case of Strongyloidiasis

	60 minutes	75 minutes	90 minutes
Time of removal	60 minutes	75 minutes	90 minutes
Amount aspirated	10 cc.	15 cc.	60 cc.
Free hydrochloric acid	0	16	10
Combined hydrochloric acid	8	26	16
Organic acids	12	14	28
Total acids	20	56	54
Blood	0	0	0
Mucus	1 plus	1 plus	2 plus
Bile	0	0	0

REPORT OF CASE

History.—A single woman aged 33, born and reared on a farm, had the usual diseases of childhood without complications, and at 19 appendicitis with rupture before operation and a slow convalescence covering some twelve months. The menses began at 13 and continued normally. Her maximum weight was 128 pounds (58 Kg.) at 25; her current weight ranged from 98 to 100 pounds (44.5 to 45.4 Kg.).

She was seen in consultation with Dr. J. C. Hartman, the family physician, and Dr. Lamar Neblett, surgeon, having been admitted to St. Anthony's Hospital with a tentative diagnosis of "surgical abdomen." She had been ill for one year, with a poor appetite, nausea, occasional vomiting, unlocalized pain in the abdomen, abdominal distention and tenderness of a low grade, loss of weight and strength, a tendency toward constipation and an almost daily headache.

Examination.—She appeared undernourished with dry, atonic skin and flaccid muscles. There was low grade cervical adenopathy. An adenoma was present at the junction of the isthmus and the left lobe of the thyroid. The lungs showed no active abnormality. There were no neurologic signs of diagnostic significance. There was a marginal infection of the gums, and the tonsillar crypts contained cheesy exudate. Generalized abdominal tenderness was present, most marked in the lower part of the epigastrium and below the umbilicus; the liver was not palpable, but there was low grade tenderness on heavy percussion. The cecal head was palpable and tender; the sigmoid flexure, spastic and tender. Peristalsis was audible and accentuated by palpation. By percussion the spleen measured 8 by 9 cm.

Urinalysis showed no abnormality except an occasional hyaline cast. A blood count showed 4,200,000 erythrocytes, 14,800 leukocytes and 85 per cent hemoglobin; the color index was 1, and there were 62 per cent polymorphonuclears, 24 per cent lymphocytes and 14 per cent eosinophils. The results of fractional gastric analysis after a test meal are shown in the accompanying table.

The duodenal contents showed Strongyloides larvae (motile) and adult worms; the feces (obtained by saline purgation), Strongyloides (actively motile) and occult blood.

Clinical Course.—Thymol, carbon tetrachloride, santonin, oil of chenopodium, dihydranol and gentian violet were used in turn. With some the duodenal contents showed a disappearance of larvae for a few days only, with as many appearing at subsequent study as before treatment. Observations were made in the laboratory to determine the killing strength of some, in fact most, of these chemotherapeutic substances. Solutions of salicylic acid (1:100) lessened motility definitely, but complete cessation was not obtained if the specimen was kept on a warm stage. Iodine was then tried, and an almost spectacular change was noted in less than one minute. The worm would rapidly lose motility and straighten out and could not be restored. There was little difference in effectiveness between tincture of iodine and compound solution of iodine. The latter was selected for use. It was given through a transduodenal tube. Larvae recovered from the duodenum and in the feces were motionless and eventually determined to be lifeless. This proved only a temporary disappearance, however, as larvae were recovered when the patient returned in two weeks. The term temporary disturbance is emphasized, for in this patient and four other members of her family adult worms and larvae were again found in two weeks. Only after a thorough clean-up campaign, followed by a course of compound solution of iodine given by tube, were permanent negative results charted.

The patient gained weight, from 105 pounds (47.6 Kg.) on discharge from the hospital to 129 pounds (58.5 Kg.) in April 1936.

SUMMARY

Strongyloidiasis is a more frequent infestation than the profession appears to believe.

Its diagnosis rests ultimately on the finding of parasites or larvae in the duodenal contents and feces.

Iodine has been found the most satisfactory agent for removal of the worms.

A series of nine cases were studied as a basis for the conclusions reached on the efficacy of treatment.

The criteria on which the conclusion of permanent riddance of infestation was based were repeatedly negative results of study of the duodenal fluid and feces.

ABSTRACT OF DISCUSSION

DR. THOMAS T. MACKIE, New York: Dr. Simpson did not have time to discuss certain important aspects of the life cycle of this parasite. The adult female penetrates the mucosa of the intestine, often creating extensive tunnels in the host tissue. These are superficial to the muscularis mucosae. Viable larvae are produced which usually are passed in the stools as the rhabditiform or noninfective form. The infective filariform larvae may likewise be produced in the host's intestinal tract. These invade the tissue, are transported to the lungs by the blood stream and ultimately reach the intestine by way of the esophagus and stomach when they grow to maturity. There is therefore the possibility of continuous hyperinfection. A parasite capable of producing such anatomic changes in the intestinal mucosa from duodenum to rectum may be responsible for disease. Unfortunately, most if not all of the studies of the clinical significance of this parasite have been insufficiently controlled. Persons harboring the strongyloides have necessarily been exposed to infection by numerous other intestinal parasites, helminthic and protozoal, to say nothing of bacterial. I have seen many

infected persons in Central America. Without exception they presented mixed infections, harboring in addition ascarids, hookworms and various types of protozoa. I have not seen intestinal disease which could with certainty be ascribed to strongyloides infestation. It is highly important to continue the clinical studies of this infection. They must be controlled by complete studies of the helminthic and protozoal load and by cultures for pathogenic bacteria. Although I do not feel competent to discuss therapy of this infection, it is relevant to point out that certain combinations of iodine are relatively efficient amebicides.

MANAGEMENT OF PROSTATIC DISEASE IN PERSONS PAST 75

A REPORT OF SEVENTY-FIVE CASES WITH END RESULTS

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In a recent paper read before the Wisconsin Urological Society on transurethral prostatic resection for bladder neck obstruction, I discussed the general problem of prostatic disease. I also carefully analyzed 100 consecutive cases of resection and compared them with 100 cases of total enucleation. The mortality rate was a flat 2 per cent for the resection group, and, remarkably enough, the two deaths occurred in relatively young men, aged 61 and 65, respectively. There were no deaths among the fifty-two patients over 70. This was encouraging and argued strongly for resection for the aged person with prostatic disease, particularly in view of the repeatedly proved fact that the mortality in any enucleation group rises sharply after the age of 70 (in my series of 100, up to 18 per cent).

The very aged, who formerly preferred either to carry on with their suffering or, in many cases, to continue with catheterization, are now seen in the urologic wards of hospitals as willing patients, electing resection rather than continuance of the uncomfortable and ofttimes painful existence which inevitably led to death. The surgeon who formerly refused to operate on the aged because of the grave risk involved with prostatectomy is now confident of his ability to benefit that group through transurethral resection. As time has gone on, with subsequent improvements of technic and armamentarium and shortening of operating time, the courage and confidence of the resectionist have increased.

During 1937 I had a relatively large group of the very aged, the total being thirty-two patients over 75 years of age. The results were so uniformly satisfactory that I was prompted to analyze them in detail, particularly in view of the fact that there was only one death in the group. The analysis brings home more forcibly than ever the fact that the experience of the operator is by far the most important factor in obtaining good results with transurethral resection. Not only was there but one death in this group in 1937, but the end results were uniformly more successful and the complications more rare. For the entire series of seventy-five patients the average age was 79½ years; 35 per cent were past 80, and two were past 90.

During the early period of transurethral resection there was apparently a great deal to be learned. It became evident that the total operating time had to be cut down. To subject a man of 80 to one hour of urethral trauma is entirely too much. One should strive to operate rapidly and to finish the entire resection in from forty to fifty minutes. Loss of blood weakens the aged rapidly. A supportive transfusion shortly after the operation is helpful in combating shock. This is resorted to more frequently now than in the past. In the 1937 group 70 per cent had one or more transfusions. Adequate continued control of bleeding throughout the operation is of great importance.

Flocks's [1] and Alcock's contributions to our knowledge of the blood supply of the hypertrophied prostate have been used to advantage in operative technic. By cutting downward deeply at 7 o'clock and at 5 o'clock to the floor of the bladder, one is in a position to fulgurate the large feeding arteries to the subcervical portion and the middle lobe of the hypertrophied gland. The remaining intravesicular projections, except the anterior lobe, then become relatively avascular. In my experience the most difficult hemorrhage to control is that which occurs at the apex of the prostate, near the verumontanum. Cutting here is deferred until the very last of the operation, after all other bleeding is stopped. Occasionally in my efforts to make lateral excavations I have cut into the surgical capsule of the prostate. In so doing one may encounter large venous sinuses which are extremely difficult to control; in fact, on two occasions recently I could not stop the bleeding by coagulation. With this type of hemorrhage a traction bag is invaluable. The slightest traction on the bag will promptly stop the bleeding. This adjunct to the urologist's armamentarium has doubtless saved many lives. The new 5 cc. retention type of catheter has done away with adhesive tape fastenings. It permits free drainage of urethral pus incident to the presence of the catheter. Its use has become a routine.

As I pointed out in a previous paper, the irrigating fluid at the end of the operation must come back clear or a very, very pale pink. Bleeding will only obstruct the catheter and disturb the entire convalescence. Irrigations of the catheter have rarely been necessary in my experience but must always be resorted to immediately by a trained attendant if a clot obstructs the eye of the catheter. Constant uninterrupted drainage of the catheter is by far the most important single item in convalescence.

Adequate removal of all obstructing tissue is a cardinal factor of success in the management of prostatic obstruction. It is even more important with the very aged than with the younger person. Inability of the urine, usually infected, to pass freely over the cut surface of the posterior portion of the urethra leads not only to severe toxemia but frequently to sepsis and disaster. Inadequate removal necessitates a second resection in an already weakened person, which is frequently the straw which breaks the camel's back. Every effort should be made to complete the operation in one sitting. The second resection is often poorly tolerated and when necessary must be undertaken only when the patient is afebrile and definitely on the mend, not when he is going downhill. If the patient is unable to void freely, it may mean that the operator has overlooked hypertrophy of the anterior lobe. This is best diagnosed with the retrospective lens, the use of which is important to successful resection. However, obstructing tissue projecting into the very outlet of the created

1. Flocks, R. H.: The Arterial Distribution Within the Prostate Gland: Its Rôle in Transurethral Prostatic Resection, J. Urol. 37: 524 (April) 1937.

funnel near the verumontanum may also be overlooked. These obstructions result from undermining of the lateral lobes with the loop and failure to remove the prostatic tissue high in the lateral lobes low down in the posterior portion of the urethra. When the catheter is removed, they fall downward into the apex of the cone. In my early experience, for fear of injuring the external sphincter I made this error frequently. Hyperplastic prostatic tissue in cases of large adenoma may bulge into the posterior part of the urethra from the lateral lobes, even after what appears to be a large and adequate resection (from 30 to 50 Gm.). As Flocks [2] has shown, such hyperplastic masses have been deprived of their main source of blood, the intra-urethral arteries. They not only cause partial or complete obstruction but are a common cause of continued sloughing, infection, urinary frequency and sometimes encrustations. Healing and epithelization of such bulging tissue masses is necessarily slow and accounts for many of the poor results and delayed healing. If one is to be successful, one must be radical, bearing in mind that in results the perfect resection approaches complete transurethral prostatectomy.

As I pointed out before, I make every effort to carry out an aseptic technic in the preoperative, operative and postoperative care of the patient with prostatic disease.

I am convinced that the careless introduction into the obstructed bladder of an aged man of foreign organisms to which he has no immunity is dangerous. Particularly is this true when the bladder and the posterior part of the urethra are severely traumatized, as they are by transurethral operations, when relatively ineffective drainage by catheter is used. I have no proof that an aseptic technic speaks for less severe reactions and the avoidance of pyelonephritis, because so many other factors are involved in the evaluation of results, but the rationale is sound.

It had long been my routine to place all prospective subjects for resection on methenamine and ammonium chloride on entry to the hospital. In June 1937 I changed to sulfanilamide as a routine drug. Each patient is given 40 grains (2.6 Gm.) each day with sodium bicarbonate, and the drug is given throughout the preoperative and immediate postoperative period. If symptoms of toxemia, such as languor, lassitude, cyanosis, weakness, tinnitus, chills and fever, set in, the drug is withdrawn. It is sometimes difficult to differentiate between fever caused by trauma and infection in the urinary tract and fever caused by the administration of sulfanilamide. If the fever is caused by the drug alone, the temperature usually subsides within twenty-four hours after the withdrawal of the drug. I have not yet any definite proof with regard to the value of sulfanilamide as a prophylactic drug against infection following transurethral operations, but I am of the distinct impression that the patients do better; the margin of safety seems greater, the reactions less severe and the incidence of pyelonephritis less. The drug has been found of distinct value late in convalescence in clearing up infection after sloughing has stopped. Other observers, however, reporting large series of cases, have found sulfanilamide of no value as a prophylactic drug against infection and sepsis.

2. Flocks, R. H.: Local Repair Following Transurethral Prostatic Resection: Its Rôle in the Clinical Events Associated with This Operation, J. Urol. **40**: 208 (July) 1938.

There is still some controversy with regard to preoperative drainage. In the presence of impaired renal function caused by back pressure, improvement after drainage is spectacular and must be carried out before resection is attempted. Furthermore, in the presence of infection with fever, drainage must be instituted. Indiscriminate catheterization or allowing a catheter to remain in the urethra can only do harm to the patient with good kidney function. It has been shown by Cabot and Meland [3] that after a catheter has remained in the urethra there comes a time, usually on the fifth or seventh day, when it often serves to irritate and aggravate the usually low grade infections commonly present in the hypertrophied glands of old men. The patient begins to have fever and becomes mildly toxic. It soon became evident that the patients with good kidney function who had never been catheterized did much better than similar patients in whom drainage with a urethral catheter had been done. Resection carries with it little shock to the cardiorenal mechanism and therefore can be performed without drainage in the majority of cases (in this series of seventy-five, or 66 per cent).

A patient who has had a large, distended bladder for a long period, with elevated values for the blood chemistry, must have slow decompression, but, as Thompson has pointed out, resection can be performed successfully on patients with highly elevated values for the blood chemistry provided the daily output is abundant and the nitrogen retention products are reasonably stabilized.

One must always remember that aged persons never do well if convalescence in bed is prolonged. My patients remain in the Fowler position four hours after the operation and are out of bed the following day. On the day of removal of the catheter (second or third) they are encouraged to walk about. They must be made to eat; brandy and nourishing fluids are of value. Often if the patient starts going downhill, the battle is lost; again transfusions must be resorted to.

ANALYSIS OF SEVENTY-FIVE CASES

An analysis of the cases shows that in 92 per cent the involvement was primary while in 8 per cent it was recurrent. Three recurrences followed a Caulk cautery punch procedure elsewhere; two followed resection elsewhere, and one followed perineal prostatectomy in 1919, suprapubic enucleation in 1924 and finally, after complete obstruction, transurethral resection in 1935.

Preoperative complications were not unusual. Thirty-nine per cent of the patients showed symptoms of uremia with elevated nonprotein nitrogen levels; 67 per cent had grossly infected glands without fever, 22 per cent had infected glands with fever and 11 per cent had clean glands; 32 per cent of the patients came to the hospital with complete obstruction, and 66 per cent were operated on without preliminary catheter or suprapubic drainage.

Microscopic section showed 27 per cent of the lesions to be carcinoma. The average stay in the hospital for all cases was sixteen days. The average amount of tissue removed was 15.08 Gm. Seventy-two per cent of the patients had one resection and 23 per cent two resections.

3. Cabot, Hugh, and Meland, E. L.: The Problem of Drainage in Preparation for Operations for Prostatic Obstruction, Proc. Internat. Assemb. Inter-State Post-Grad. M. A. North America, 1932.

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Operative and postoperative complications were common during the first three years of my experience. In four cases of hemorrhage reoperation was required for control of bleeding.

The immediate hospital mortality rate was 5.3 per cent (four patients). One death was due to perforation of the bladder (seen post mortem), one to bronchopneumonia on the tenth postoperative day (seen post mortem), one to pyelonephritis six weeks after operation (seen post mortem).

Eight patients died within one year after leaving the hospital; three of them had carcinoma and died of cachexia. Heart disease claimed two patients, and carcinoma of the stomach and bowel caused the death of the remaining three of this group.

Nine patients have since died of varying causes. Satisfactory function of the bladder was obtained in all cases of this group.

Summary of Fifty-Four Questionnaires

1. Are you satisfied with the present condition of your bladder?
   51 answered yes
   3 answered no { 1, incontinent; 1, partially incontinent; 1, with frequency }
2. Does the urine flow freely?
   51 answered yes
   3 answered no { R. Operation, 1936; S. Operation, 1937; G. Operation, 1935 }
3. How many times do you get up at night?
   4 omitted to answer
   6 answered not at all
   44 answered average 2.4 times
4. Is urination painful to you?
   46 answered no
   5 answered yes
   3 answered slightly { 1, benign disease; 2, carcinoma }
5. Is your general health improved since operation?
   40 answered yes
   2 answered no (carcinoma)
   12 omitted to answer
6. Have you gained or lost weight since operation?
   2 answered lost
   17 answered same weight
   28 answered gained (average 15 pounds [6.8 Kg.])
   7 omitted to answer

Fifty-four of the seventy-five men are still living. Each was sent a questionnaire, and, remarkably enough, answers were obtained from each patient. These are shown in the accompanying table.

CONCLUSIONS

A satisfactory result with the aged patient with prostatic disease depends largely on the skill and experience of the operator. Urethral trauma must be minimized by shortening the operating time; hemorrhage must be under control at all times. Supportive blood transfusions should be given more frequently than to younger patients (70 per cent of my group in 1937 received one or more transfusions). Whenever possible, the entire obstruction should be removed in one sitting; a second resection is often poorly tolerated. Asepsis, adequate removal of all obstruction and meticulous care of the draining catheter are even more important in older than in younger patients. I believe that sulfanilamide as a preoperative prophylactic drug against infection is of value. Despite the fact that men over 75 with prostatic obstruction are a precarious lot, resection does hold for them relief from suffering and a comfortable life so far as the bladder is concerned. There will always be a mortality rate, but with care and proper management it can be kept surprisingly low.

Clinical Notes, Suggestions and New Instruments

RECURRENCES OF UNDULANT FEVER (BRUCELLOSIS) FOLLOWING THE ADMINISTRATION OF SULFANILAMIDE

W. TURNER BYNUM, M.D., CHICKASHA, OKLA.

Within the past year ten articles in the American and British literature have come to my attention, all reporting uniformly good results in the treatment of undulant fever with sulfanilamide, no case of failure having been recorded. Because of this, and because of the unusually small number of cases reported in any series, along with the danger of the indiscriminate use of this remedy and the belief that a word of warning should be voiced to prevent the overenthusiastic employment of this procedure, I report six cases which have been unsuccessfully treated with large doses of this drug as described in the aforementioned articles:

REPORT OF CASES

CASE 1.—A white man aged 28 entered the clinic May 3, 1938, complaining of chills, fever, fatigue and aching in the lower part of the back and the calves of both legs.

The patient was a dairy worker and stated that it was his custom to "clean up" the cows, without the use of rubber gloves, after they had aborted; he had carried out this procedure several times during the past year, the last time being about April 1. He also stated that he had drunk a good deal of milk given by infected cattle.

For the two weeks preceding entrance he had had chills and fever at irregular intervals of from twenty-four to forty hours. For the past week he had been unable to perform his duties because of marked weakness, aching and fever.

The patient was fairly well developed; he was lying quietly on the examination table, mentally alert and cooperative. The temperature was 98.2 F., the pulse 84, the blood pressure 114 systolic, 80 diastolic. He weighed 155 pounds (70 Kg.). The skin was moist and warm. The eyes and ears were normal. The mouth showed evidence of oral neglect with pyorrhea of several teeth. The tonsils were submerged and cryptic; the pillars were not injected. The thyroid was not palpable. The heart and lungs were normal on auscultation and percussion. The abdomen was normal. The reflexes were physiologic. The extremities were normal.

At 4 p. m. on the day he was hospitalized the patient experienced a chill and his fever mounted to 103.8 F. and returned to 99 F. at 10 o'clock.

Laboratory examination revealed the following: The red blood count was 4,320,000, hemoglobin content 14 Gm., white blood count 5,100. The Kahn reaction was negative. The sedimentation rate was 7 mm. in one hour. Undulant fever agglutination was 4 plus in all dilutions to 1:480. The tuberculin reaction was negative with purified protein derivative. The cutaneous test was markedly positive to 60,000 Brucella abortus and Brucella melitensis organisms.

Following a second chill and fever to 103 F. the patient was placed on sulfanilamide and given 450 grains (30 Gm.) in eleven days, as follows: first day 60 grains (4 Gm.), second, third and fourth days 80 grains (5 Gm.), fifth day 60 grains, sixth day 40 grains (2.6 Gm.) and then 10 grains (0.65 Gm.) for five days. The temperature became normal and the patient felt markedly improved on the fourth day. He continued to improve and had no further fever for five weeks, at which time he had a chill and was reported to have a fever as high as 105 F. Following this he had a return of chills, fever, malaise and aching, recurring at irregular intervals as before. He was again placed on sulfanilamide as previously, which was likewise accompanied by a remission of symptoms on the fourth day. Immediately after his course of sulfanilamide he was given atabrine 5 grains (0.3 Gm.) three times a day for five days on the advice of another physician. Following this the patient was not heard from for three months, but inquiry at this time disclosed that he had recently had a return of his symptoms and was at that time "taking treatment" from an Indian faith healer who "had his temperature down one degree."

CASE 2.—A white man aged 26 was brought to the hospital June 4, 1938, in a delirious state and with a temperature of 105 F. The history given by relatives at this time disclosed the following significant facts: The patient had recently been on a fishing trip in an endemic malarial country and had been drinking much milk from a cow known to be "Bang positive."

On physical examination the patient was asthenic, irrational and thrashing about in bed. The blood pressure was 142 systolic, 70 diastolic; the pulse was 126, the temperature 105 F., the respiratory rate 18. The examination was otherwise essentially negative. Laboratory examination revealed red blood cells 4,850,000, hemoglobin 14.5 Gm., white blood cells 8,250. The sedimentation rate was 6 mm. The Widal reaction was negative. Thick smears taken at the height of fever were negative for malarial parasites. The Kahn reaction was negative. Undulant fever agglutination in dilutions of 1:60 was 4 plus, of 1:120 4 plus, of 1:240 3 plus and of 1:480 2 plus. The cutaneous test was markedly positive for undulant fever. Roentgenograms of the chest were negative.

After three days, with two subsequent chills and intermittent fever to 103.2 F., a diagnosis of undulant fever was made and the patient was given sulfanilamide 450 grains in six days, then 20 grains (1.3 Gm.) a day for five days and 10 grains a day for one week.

The patient had chills and fever for three days following institution of treatment and continued to have an intermittent but gradually diminishing daily elevation of temperature of about 2.5 degrees F. for seven days. At this time it was found that the patient's hemoglobin content was reduced to 11.5 Gm., and a transfusion of 550 cc. of whole citrated blood was given and medication was continued.

The patient apparently made an uneventful recovery, gained weight and felt well for three weeks after discontinuance of treatment; then there was a return of symptoms of intermittent fever, anorexia and weakness. The patient was advised to take vaccine treatment, which he did for two weeks, but discontinued this because of his belief that vaccine was aggravating the condition.

CASE 3.—A nurse aged 23 consulted me July 2, 1938, because of "waves" of mental depression, malaise and fever to 100.5 F., which had occurred at irregular intervals of from two to four days for six weeks. The patient was known as a "great milk drinker" and had drunk milk from a number of different sources, some raw, but none known to be from infected cattle.

The patient was well nourished, plump and alert. The temperature was 100 F., the pulse rate 96 and the blood pressure 106 systolic, 70 diastolic. The mouth was well kept, with tonsil tags at both bases. The heart, lungs and abdomen were normal. Pelvic examination was essentially negative. The red blood cells numbered 4,200,000, the hemoglobin content was 14 Gm. and the white blood count was 4,680. Undulant fever agglutination was 4 plus in all dilutions. There was a markedly positive cutaneous reaction with 5,000,000 Brucella abortus and Brucella melitensis organisms. The percutaneous tuberculin reaction was mildly positive. X-ray examination of the chest was negative. The patient was given 450 grains of sulfanilamide in ten days, 350 grains in the first five days. She continued her duties but malaise and aching persisted, although she had a remission of fever after the seventh day. The fever returned eighteen days after discontinuance of treatment and continued for ten days, when the patient was placed on vaccine treatment in very small daily doses, which frequently gave marked local and mild general reactions, but she was markedly improved after two months of continuous treatment by vaccines and has remained free from fever to date, Nov. 7, 1938.

CASE 4.—A white woman aged 38, a nurse, consulted me July 18, 1938, complaining of alternating periods of exhilaration and depression, "waves" of fatigue and anorexia, associated with pain and swelling in the middle and ring fingers of the right hand and some rather vague generalized aches and pains throughout the body, of four or five months' duration. The patient lived in a district where Bang's disease was prevalent, had drunk milk from many sources but had had no direct contact with infected cattle.

On physical examination the temperature was 99.6 F., the pulse rate 60, the blood pressure 100 systolic, 70 diastolic, but examination was otherwise essentially negative. Laboratory examination August 17 revealed the sedimentation rate to be 12 mm., hemoglobin 16 Gm., red blood count 5,600,000. Gastric analysis revealed free hydrochloric acid 12, total acid 28. Undulant fever agglutination was negative. The basal metabolic rate was plus 5 per cent. X-ray examination of the chest, stomach and colon was negative and of the right hand revealed evidence of periostitis of the affected fingers. The intracutaneous tuberculin test gave negative results. The intracutaneous test for undulant fever with 60,000 Brucella abortus and Brucella melitensis organisms gave the largest reaction that I ever observed with a like amount of vaccine, the redness and induration extending from the cubital fossa to within 2 inches of the flexor surface of the wrist and persisting in this condition for ten days, following which a suppurating abscess formed which drained for eight weeks.

The patient was seen in consultation by three other physicians and a diagnosis of undulant fever was agreed on and sulfanilamide therapy instituted August 17, 380 grains (25 Gm.) being administered in five days and 10 grains a day for ten days. The patient was last seen October 15, at which time she stated that she had noted no improvement in her general condition, had continued to have subjective symptoms but was more interested at the time in a lump in the breast for which surgery was advised, but the patient has not been heard from since.

CASE 5.—Dr. H. M., a man aged 34, an associate of mine, had been complaining of recurrent transient attacks of fatigue, anorexia, depression, somnolence and generalized aching lasting from a few hours to two days and recurring at irregular intervals for several months and associated with a sensation of fever.

The patient was robust with no physical abnormalities, having a temperature of 99.8 F., a pulse rate of 76 and a blood pressure of 120 systolic, 80 diastolic. Laboratory examination August 18 was as follows: Undulant fever agglutination was 4 plus in all dilutions to 1:400. The intracutaneous tuberculin test gave negative results. The Kahn reaction was negative. A definitely positive cutaneous reaction with Brucella abortus and Brucella melitensis persisted for two weeks.

The patient took sulfanilamide 20 grains the first day, 80 grains a day for three days and then from 20 to 40 grains a day for two weeks beginning August 20. At the end of this time he discontinued treatment and stated that he could not distinguish any change in his subjective symptoms. September 16 he was again found to have a 4 plus undulant fever agglutination and was advised to try the vaccine treatment, which was instituted at this time and has been continued to date, with marked improvement of all symptoms.

CASE 6.[1]—A man aged 21 who consulted Dr. T. L. Wainwright of Oklahoma City July 24, 1938, complained of marked weakness, malaise, generalized aching and dyspepsia. The patient gave a history of having taken over 1,000 grains (65 Gm.) of sulfanilamide in daily doses of 60 grains from June 24 to July 10, 1938, for the treatment of gonorrhea.

The patient was given a thorough examination by Dr. Minard F. Jacobs, also of Oklahoma City, and Dr. Wainwright. He was well developed. The temperature was 100.2 F., the blood pressure 106 systolic, 72 diastolic, and the pulse rate was 120. There were no other physical abnormalities save for tenderness throughout the abdomen, especially in the midepigastrium. He was found to have a markedly increased phagocytosis for Brucella melitensis, as shown by the opsonic index, a 4 plus undulant fever agglutination and a negative Kahn reaction.

The patient was placed on daily injections of undulant fever vaccines and has made marked and consistent improvement in all symptoms.

SUMMARY

Two cases of acute, one of subacute and three of chronic undulant fever—five from my personal practice and one from that of Dr. T. L. Wainwright—have been treated by maximum therapeutic doses of sulfanilamide as recommended in the American and British literature of the past year. I have been unable to duplicate the satisfactory results heretofore reported in this condition by the use of this therapeutic agent.

1. Wainwright, T. L.: Personal communication to the author.

DERMATITIS DUE TO BUTYN

HOWARD J. PARKHURST, M.D., AND JOHN A. LUKENS, M.D.
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According to Lundy [1] "Good surface anesthetics are not common. One that is used with considerable satisfaction is butyn. It is used as a surface anesthetic in 2 per cent solution. It is used for anesthetizing the throat and nose by spraying, a small amount of 5 or 10 per cent solution being used. In a 5 or 10 per cent solution as a spray, butyn takes the place of a 10 to 20 per cent cocaine spray for anesthetizing the throat and larynx prior to the introduction of the intratracheal tube under general anesthesia. Butyn is also used with considerable satisfaction by ophthalmologists in an ophthalmic ointment of 2 per cent concentration.

"In the use of butyn one should be on guard for idiosyncrasy, since occasions have developed when it seemed that the patient was hypersensitive to butyn. The butyn solution is somewhat irritating when instilled into the eye, and for that reason it has not become as popular as it would have otherwise. It may be used in gels and ointments, in 0.5 or 1 per cent concentration. Butyn is not habit forming."

Since Lundy mentioned the possibility of idiosyncrasy, we had expected that numerous cases of dermatitis due to butyn would have been reported. However, in a careful search through the literature, only three such cases could be found.

In 1924 Greenwood and Quest [2] of Boston reported a case of dermatitis due to butyn, beginning on the hands and arms and becoming generalized. The patient was a urologist who used a 2 per cent solution of butyn with epinephrine as a local anesthetic for passing sounds, for cystoscopic study and for minor operations. Cutaneous tests with this solution were strongly positive (and tests with a 1 per cent solution of procaine hydrochloride were also [less markedly] positive).

In 1927 Lemoine [3] of Kansas City, Mo., and Newton [4] of Dallas, Texas, each reported a case of conjunctivitis and dermatitis due to butyn. Both patients were women (aged 50 and 66). Lemoine's patient, aged 50, had used a solution containing 1 per cent butyn and 0.25 per cent zinc sulfate in her eyes with no apparent ill effects. Seven months later she used the same solution again, and severe conjunctivitis and dermatitis of the lids immediately followed. An intradermal test with 1 per cent solution of butyn was strongly positive, and the conjunctivitis and dermatitis recurred later when this solution was instilled in the eyes. For the local treatment of bilateral glaucoma simplex, Newton prescribed a solution of pilocarpine containing 1 grain (0.06 Gm.) each of butyn and ethylmorphine hydrochloride to the ounce, for home use. A marked dermatitis of the eyelids ensued, faded when the butyn was discontinued and recurred within thirty minutes after 4 per cent butyn was used as an anesthetic for taking the tonometric reading.

REPORT OF CASE

Sept. 7, 1938, one of us (J. A. L.) saw Mrs. O. C. T., aged 49, with a sty of the right upper eyelid and an infected chalazion of the right lower lid. A 2 per cent solution of butyn was instilled in the eye for local anesthesia, and after three instillations the usual chalazion clamp was applied to the lower lid and the infected chalazion was incised. Pus was expressed and granulation tissue curetted away, and the cavity was then wiped out with a cotton-tipped applicator saturated with a 1:1,000 solution of merthiolate. The clamp was then removed and the eye bathed with hot compresses to control bleeding and swelling. The patient was instructed to continue the hot compresses at home and to use drops of 0.2 per cent solution of zinc sulfate in 2 per cent boric acid three times a day. September 8 both right eyelids were markedly swollen and itched severely. The drops and compresses were continued, and paste of zinc oxide (without salicylic acid) was prescribed for local application.

September 9 there was a more severe dermatitis of the lids, with vesiculation and edema; the eye was swollen shut. An erythematous vesicular streak, about 5 mm. wide, extended down the cheek to the chin, apparently following the path along which a solution had run down. The patient was advised to wash the area night and morning with mild soap and water and to apply moist compresses of a saturated boric acid solution constantly during the day and at night a little plain zinc oxide ointment, rubbed in gently and wiped off with cotton, followed by the application of a little plain talcum. The dermatitis subsided almost completely in a week. In the meantime patch tests with the solution of butyn and with the zinc sulfate solution were applied to the patient's left arm September 10 and removed twenty-four hours later. The reaction to the butyn was positive and increased in intensity, so that three days later the patch was red, vesicular and edematous and the arm swollen and painful. Calamine lotion was ordered, and at the end of a week this reaction had subsided.

This patient showed an intense hypersensitivity to butyn as used in ophthalmologic practice. Perhaps such instances occur more frequently than the paucity of reports would seem to indicate.

316 Michigan Street.

1. Lundy, John S.: The Use of Local Anesthetics, J. A. M. A. **107:** 1468 (Oct. 31) 1936.
2. Greenwood, Arthur M., and Quest, James F.: A Case of Butyn Dermatitis, J. A. M. A. **83:** 1077 (Oct. 4) 1924.
3. Lemoine, Albert N.: Conjunctivitis and Dermatitis Due to Butyn, Am. J. Ophth. **10:** 125 (Feb.) 1927.
4. Newton, F. H.: Conjunctivitis and Dermatitis Due to Butyn, Am. J. Ophth. **10:** 432 (June) 1927.

Special Article

CONFERENCES ON THERAPY

TREATMENT OF EDEMA

NOTE.—*These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital. The questions and discussions involve participation by members of the college staff, students and visitors.*

DR. EUGENE F. DU BOIS: It was only ten or fifteen years ago that there were large numbers of patients in medical wards with extreme grades of edema. They presented a distressing picture. Treatment was most unsatisfactory. Nowadays such patients are relatively few, thanks to the various studies in physiology, biology, chemistry, pharmacology and clinical medicine. Dr. Milhorat will begin the discussion.

Normal Values

Water content of human body from 58 to 66 per cent of the body weight
Blood volume of human body from 79 to 99 cc. per kilogram of body weight
Volume of lymph from 1,500 to 2,400 cc.
Osmotic pressure of blood serum 30 mm. of mercury
Total serum protein from 6.5 to 8.2 per cent
Total serum albumin from 4.6 to 6.7 per cent
Total serum globulin from 1.2 to 2.3 per cent
Osmotic pressure of serum albumin is four times that of serum globulin
Hydrostatic pressure:
Arteries 120 mm. of mercury
Capillaries from 20 to 26 mm. of mercury
Veins 6.7 mm. of mercury.
Sweating in normal adult male:
At rest, from 23 to 30 C., skin and lungs. From 29 to 33 Gm. per kilogram
At rest, from 30 to 35 C., skin and lungs. From 100 to 120 Gm. per hour
Vigorous muscular exercise up to 230 Gm. in 12 minutes, 800 Gm. in 35 minutes

DR. A. T. MILHORAT: Edema is a symptom and sign, not a disease. Various and diverse are the factors which can bring it about. Some of these factors are still obscure but many of them are now fairly well known, such as the role of blood proteins, of the p_H of the tissues and of potassium and sodium ions, and the effect of salt on the osmotic pressure of proteins. Through analysis of these and others we are able to comprehend better the treatment of edema and the successful results as well as the failures.

Some of the mechanisms that cause edema are:

1. Increased permeability of the capillary wall (snake venom, asphyxia).

2. Decrease in the osmotic pressure of the blood, as after plasmapheresis and repeated hemorrhage and in cases of massive albuminuria. The thinner fluid, one might say, is drawn into the tissues.

3. Increased hydrostatic pressure in the vessels of the region involved (cardiac failure, varicose veins). In this case it might be said that the fluid is forced into the tissues.

4. Retention of certain substances the accumulation of which disturbs the normal osmotic relationships between the blood plasma and the tissues. Edema arising as the result of the use of sodium chloride in patients with impaired capacity for its excretion is an illustration of this fact.

There are several clinical varieties of edema: cardiac, renal, nutritional, toxic, obstructive. Each presents its own peculiar problems in treatment. The factors which require consideration in every case of edema are (1) diet (protein content, acid or alkaline ash), (2) fluid intake, (3) salt intake, (4) diuretic agent and (5) special measures directed to the underlying disease itself.

In most cases of heart failure digitalis suffices to abolish edema indirectly by improvement of the circulation through the kidney. There are many cases, however, in which that is not enough, and in these some of the diuretics alone or in combination often produce dramatic results. The more important diuretics are (1) the purine bases, or xanthines, (2) the organic mercurials, (3) the acid-forming diuretics and (4) nonthreshold diuretics.

The purine bases or the members of the caffeine group have long been used as diuretic agents but are perhaps not so popular today as some of the others. The use of caffeine itself is limited by the fact that it tends to cause restlessness and insomnia. In theobromine and theophylline the diuretic action is stronger and they exert relatively less stimulant effect on the higher centers. These compounds are insoluble in water but go into solution readily when mixed with such salts as sodium acetate, sodium salicylate or calcium salicylate. The insoluble theophylline (theocine) may be used as such in oral doses varying from 1½ to 9 grains (0.1 to 0.6 Gm.) three times daily. It tends to irritate the gastrointestinal tract and vomiting is caused in some individuals by even small doses. The soluble double salts (theobromine with sodium salicylate, theophylline with sodium acetate or theobromine with calcium salicylate) are said to be less irritant but the evidence is not conclusive. Only about 50 per cent of their weight is the purine base. The double salt of theophylline is given in doses of about 3 to 15 grains (0.2 to 1 Gm.) three times daily, those of theobromine in doses of from 15 to 30 grains (1 to 2 Gm.) in a similar way. Theophylline with ethylene diamine (aminophylline) is also effective in comparable amounts; it contains somewhat more of the base, namely about 75 per cent of its weight. How the purines act to produce diuresis is not fully established. Various views have been advanced: increased renal blood flow, some extrarenal action, or direct action on the renal epithelium. Increase in glomerular filtration appears to be the outstanding phenomenon.

The most effective diuretics in use at the present time are the organic mercurials. There are several such preparations. The older merbaphen (novasurol) has now been virtually replaced in practice by mersalyl (salyrgan). Other similar preparations are neptal and mercupurin. All of these exert essentially similar actions. They are supplied on the market in ampules in which 1 cc. of the solution represents approximately 40 mg. of mercury in nonionizable form. There is available a rectal suppository known as mercurin and another of salyrgan. These contain much larger amounts of mercury and sometimes cause rectal irritation. They are useful, however, in cases in which the frequent injection of a drug is not feasible. The dose of the solutions of these mercurials in the treatment of cardiac edema is from 1 to 2 cc. by intravenous injection. They are sometimes given intramuscularly but are liable to cause pain at the site of injection. Great care must be taken to avoid leakage into the subcutaneous tissues, for this will cause local necrosis and slough. The use of a very small needle for the intravenous injection helps to prevent this. The interval between doses varies greatly, depending on the severity of the edema. Usually an injection every second or third day suffices; sometimes a daily injection is necessary; often an injection once a week will prove sufficiently effective. As a rule, the necessary dosage for maintaining a patient free from edema causes no appreciable injury to the kidney, although occasionally patients unduly sensitive to the action of mercury are encountered, and these may show signs of mercury poisoning: renal damage, stomatitis, vomiting and bloody diarrhea. It is wise, therefore, to make frequent urine examinations for the presence of blood cells and for increase in albumin or casts during a course of treatment. The mechanism of the diuretic action of the organic mercurials is not established. In contradistinction to the xanthines these are generally believed to act primarily by decreasing tubular reabsorption.

An acid-forming diuretic, such as ammonium chloride, is often administered together with the organic mercurial. As I shall mention presently, increased acidity of the tissues favors diuresis; also a normal blood chloride is necessary for effective diuresis. The majority of cases, however, do quite well with the mercurial alone.

There are several compounds belonging to the group of so-called acid-forming diuretics, such as calcium chloride, ammonium chloride and ammonium nitrate. These substances, when given in large amounts, shift the acid-base equilibrium of the body toward the acid side. In the case of ammonium chloride the chemical reaction involves the conversion of ammonia to urea with the liberation of the acid ion. In the case of calcium chloride the reaction with carbonic acid produces calcium carbonate and hydrochloric acid. The diuretic action is due not solely to the acidity, however, but also to the character of the acid radical, for in some cases ammonium chloride, in other cases ammonium nitrate proves more effective.

Ammonium chloride and ammonium nitrate are among the most useful members of this group. They are used in total amounts of about 6 Gm. daily given in single doses of 2 Gm. three times a day. A convenient form is a tablet coated with phenyl salicylate of 0.5 Gm. each.

Urea is a nonthreshold substance which the kidney excretes as soon as it enters the blood stream and it takes with it quantities of water. It has been used in various types of edema with favorable results for about half a century. It is sometimes useful in patients with nephritic edema in whom the blood urea is not elevated, but the most striking effects are seen in patients with

cardiac edema. Large doses are necessary, namely from 30 to 60 Gm. daily given in single doses of from 10 to 20 Gm. three times a day. It has a disagreeable metallic taste and sometimes causes vomiting. It is best given after meals, well diluted with water or orange juice. Excessive doses cause weakness and lassitude, associated with very high blood urea values (from 80 to 90 mg. per hundred cubic centimeters).

The diuretic effect of the purine bases, the organic mercurials and urea begins within a few hours after the dose, and the effect of any given dose is usually over within approximately twenty-four hours.

The accumulation of sodium in the tissues tends to promote the accumulation of water. The administration of potassium salts, however, tends to increase the excretion of sodium. Potassium salts, therefore, are occasionally very effective as diuretics. Potassium nitrate is the compound generally employed, in doses of about 5 Gm. daily. It sometimes produces a marked diuresis in patients in whom other agents have proved unsuccessful. The potassium ion is more toxic than sodium and in the presence of severe renal injury potassium salts must be given with caution, since the kidney may fail to eliminate them adequately, in which case the potassium concentration of the blood may rise to toxic levels.

The restriction of salt intake in patients with edema is usually desirable. When the ability to excrete salt is impaired the use of salt sometimes causes a rapid increase in the edema and, conversely, the restriction of salt may be followed by a decrease in the edema.

The restriction of water involves several considerations. It is usually advisable to restrict the fluid intake to about a liter a day. However, excessive restriction of water may prove injurious. Newburgh showed that patients with impaired ability to concentrate the urine will often show a decrease in edema when the fluid intake is increased. He believes that enough water should be given so that the specific gravity of the urine is kept below the maximal specific gravity of which the kidneys are capable. Normally the kidneys require around 600 to 700 cc. of water daily to excrete the waste products. Patients with an impaired ability to concentrate the urine require larger amounts of water. For such patients restriction of fluids will increase the edema, where the administration of adequate amounts of water will decrease it.

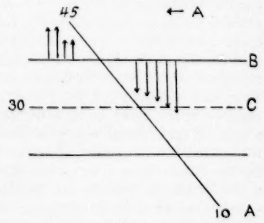
TREATMENT OF NEPHROSIS AND NEPHRITIS

DR. LEE E. FARR (of the Rockefeller Institute): In the treatment of edema, a disease which is called pure lipoid nephrosis has occupied an important experimental role because in this disease we have a process in which edema is formed in the individual without renal failure and without cardiac failure; in other words, probably here the physical-chemical mechanism for the exchange of fluid between the vascular system and the tissues is the one primarily at fault in the edema formation.

In the normal blood serum or plasma the proteins exert an osmotic pressure of approximately 30 mm. of mercury. The osmotic pressure might be simply defined as the attraction of the solute for the solvent; in other words, a plasma protein concentration of from 6.5 to 8.2 per cent, with an albumin above 4, will attract water to such an extent that 30 mm. of mercury pressure is exerted in an osmometer.

As the blood enters the capillaries the hydrostatic pressure due to the blood pressure is greater than the osmotic pressure. This difference in pressure varies with the point at which the measurements are made because there is a fall in the hydrostatic pressure as the blood progresses through the capillary system, but at approximately the arterial end of the capillaries the total hydrostatic pressure would be about 45 mm. of mercury.

Since the osmotic pressure of serum is approximately 30 mm. of mercury, that would give a pressure gradient of about 15 mm. of mercury. In other words, water tends to diffuse out of the vascular bed and into the extracellular spaces. On the other hand, farther along the capillary the hydrostatic pressure falls, so that at some point there is equilibrium, and at this point there will be equal diffusion from within the capillary out and from the extracellular spaces into the capillary. At the venous end of the capillary, with a further drop in the hydrostatic pressure, we find a negative gradient of about 20 mm., which tends to enhance the transfer of water from the extracellular spaces in the capillary bed. Under normal conditions these processes of diffusion out and in are balanced so that the full quantities of water which are extruded from the vascular bed are resorbed in the capillaries and the lymphatics. In nephrosis, which exemplifies the effects of a reduction of the serum protein, instead of there being an osmotic pressure exerted of 30 mm. there is a pressure of something less than 30 mm., depending on the reduction in protein.



Schematic representation of fall in hydrostatic pressure in a capillary and its relation to the colloid osmotic pressure of plasma, shown here as 30 mm. of mercury. The arrows represent the resultant diffusion effected as a difference in the two pressures. *A*, hydrostatic pressure; *B*, capillary wall; *C*, osmotic pressure.

With a reduction in serum osmotic pressure, a glance at the illustration will make apparent that throughout most of the course of the capillary the hydrostatic pressure is exceeding the osmotic pressure, so that diffusion of fluid from the vascular system to the extracellular spaces is enhanced, while in only a relatively short distance and at a diminished pressure gradient is fluid transferred from the extracellular spaces back into the capillary. A rise of venous pressure would exert essentially the same effect. It is purely the relationship between the hydrostatic pressure which is existing in the system at any point, tending to push the fluid out, and the osmotic pressure, which tends to withdraw fluid from the extracellular spaces.

It would seem, of course, that the ideal way to treat this condition is to increase the osmotic pressure of the blood serum or plasma. This can be done in a variety of ways. Of course, it can be done by increasing the plasma protein. Such an increase occurring spontaneously may be seen in patients with nutritional edema. With adequate nutrition being provided, the plasma proteins rise to their normal level and edema disappears. The osmotic pressure may be increased by the intravenous administration of acacia, which, being a nondiffusible substance, raises the colloid osmotic

pressure of the blood in proportion to its plasma concentration. It has been attempted by the administration of concentrated human serum and also by the administration of blood by transfusion.

In the treatment of nephrosis, however, none of these methods are particularly satisfactory. Acacia is a foreign substance, which tends to accumulate in the liver, and the ultimate effects of acacia are not entirely understood, in addition to which following the administration of acacia severe reactions may be encountered in patients, which may be of such a degree as to induce an acute uremia.

The administration of plasma protein by transfusion or concentrated serum is not satisfactory because in nephrotic individuals the extra plasma protein which is administered intravenously is lost usually within twenty-four to forty-eight hours in the urine. As a result, benefits obtained by such treatment are usually transitory, although occasionally a patient does seem to be permanently benefited.

In adults, when the plasma albumin is reduced below approximately 2.5 Gm. per hundred cubic centimeters of plasma, salt restriction and administration of diuretics such as urea are usually ineffective in controlling the edema. This, then, we take as the critical level for edema formation in adults. In children, however, the critical level is approximately 1.2 Gm. per hundred cubic centimeters of plasma. These figures are for the plasma albumin. The osmotic pressure of globulin is relatively insignificant in comparison with the albumin. Why this difference should exist between adults and children is not clear, because osmotic pressure measurements on these serums are in essential agreement with the albumin content. These are merely empirical figures which have been observed in the clinic. When a child's plasma albumin—a child around 4 or 5 years—is below 1.2, diuretic measures are not of much avail, and, when the adult's plasma albumin is below 2.5, again diuretic measures are not of much avail. However, in a nephrotic child with the plasma albumin above 1.2 Gm. per hundred cubic centimeters very often striking and remarkable results are obtained by the administration of almost any diuretic or usually simply by salt restriction.

In the attempt to build up plasma protein in these patients it has been customary to feed a high protein diet. A high protein diet has several effects: In the first place, it increases the quantity of urea which is available for excretion and thereby acts much the same as the simple administration of urea. This effect is primarily diuretic. A second effect of high protein feedings, which in children with pure lipoid nephrosis and in dogs is relatively easy to demonstrate, is what we may interpret as an increased renal blood flow reflected by an increase in the urea clearance.

With an increased renal blood flow one might expect an increase in the glomerular filtrate with a corresponding increase of water elimination. The exact mechanism is not yet worked out, but with an increase of renal blood flow and urea excretion usually more salt and water are eliminated and the effect is very roughly proportional to the quantity of protein that is fed in the diet.

The third effect, which is really what we are seeking, is to provide nitrogen for restoration of tissue proteins and plasma proteins. To promote optimal nitrogen assimilation there are certain restrictions that must be introduced in the use of a high protein diet. Nephrotic children fed 0.5 Gm. of protein per kilogram of ideal body weight can be shown to be on a negative nitrogen balance. Obviously we cannot hope for restoration of plasma protein with the patient on a negative nitrogen balance; as a matter of fact, a decrease in plasma proteins might be expected if the diet is fed for a long enough period of time. With an increase of protein in the diet, from 0.5 to 1, 2 and 3 Gm. per kilogram of ideal body weight, the children show an increasingly positive nitrogen balance and accordingly are, I believe, under conditions which tend to promote the restoration of tissue and plasma protein.

However, when the protein in the diet is increased above 3 Gm. per kilogram of ideal body weight, not only is there no further increase in positive nitrogen balance but actually there is a decrease in the nitrogen assimilated, so that a child may be on a negative nitrogen balance with a protein intake of 5 Gm. per kilogram of ideal body weight, whereas he is on a positive nitrogen balance at 3. The point at which this break in nitrogen assimilation occurs is quite sharp and is apparently at about 3 Gm. per kilogram of ideal body weight. Apparently, in children with increasing protein intakes there is a speeding up of the catabolic processes, and on a very high protein diet the nephrotic child may actually be on a negative nitrogen balance. This fact may be deceptive clinically, because with this very high protein diet the initial increase in excreted urea due to dietary protein and destroyed tissue may cause a temporary diuresis with apparent clinical improvement. Such a paradox will occur only when the plasma albumin is above the critical edema level.

In the adult we give about 1.5 Gm. of protein per kilogram of ideal body weight. It is obvious that the patient cannot be fed on his actual body weight, because he may weigh as much as 50 per cent over his expected weight. A diet calculated on his ideal body weight provides an adequate amount of nitrogen for the restoration of protein tissue with a sufficient excess provided for wear and tear quota. The actual protein fed per kilogram of protein tissue in these patients is quite high because of the severe malnutrition due to nephrosis.

The general caloric intake, of course, must be kept adequate throughout any protein-feeding period. In general, if one is desirous of controlling the edema in nephrotic patients it is best to place them on as ideal a protein intake as possible in order to promote the regeneration of tissue and plasma proteins and then if necessary to supplement this by the judicious use of diuretics. The diuretic would not be indicated until the plasma albumin exceeds the critical edema level. The permanence of any improvement will depend ultimately on the restoration of tissue and plasma proteins to a normal level and it is well to be cautious in the use of diuretics on these patients so that the physician does not delude himself into believing that the unphysiologic state attained as a result of the use of diuretics represents material improvement of the patient.

DISCUSSION

STUDENT: Does this 3 Gm. of protein per kilogram of body weight apply to both the child and the adult or only to the child?

DR. FARR: That is only in the child. In the adult we give about 1.5 Gm. per kilogram of ideal body weight because no provision is necessary for growth require-

ments in the adult. The tendency of children to go into a negative balance on a high protein intake is what we call paradoxical dumping. It occurs in normal children as well as in nephrotic children. The mechanism is not well understood. Apparently in the normal child the level at which the paradoxical dumping occurs is somewhat higher than in the nephrotic children. Probably in the normal child it is around 4 Gm. per kilogram of ideal body weight.

STUDENT: For the patient who has a retention of urea wouldn't ammonium chloride be contraindicated on the basis of its forming further urea to be excreted?

DR. MILHORAT: I think not. The ammonium chloride is given in small amounts, whereas the amount of urea normally excreted is from 20 to 30 Gm. daily. If you estimate the amount of urea formed from the ammonium chloride which is administered, it will be found to be small. I should like to know whether Dr. Farr has noticed any difference in the effectiveness of the different proteins. One would expect a difference between a protein like fibrin, which is complete, and one like gelatin, which is very unsatisfactory as a nutritive substance.

DR. FARR: It is almost impossible to give pure proteins in the diet. You cannot feed patients just gelatin or casein and get them to take it. Experimentally, apparently lactalbumin, casein and beef protein have about the same quality with regard to regeneration of plasma protein. Ox serum protein seems to surpass each of the others. That seems to be about the best protein that could be used if one is restricted to feeding a single protein; but the difference between ox serum protein and a well rounded diet with about 70 per cent of the protein in the diet as animal protein is not sufficient to warrant an attempt to feed a patient on pure ox serum protein. Experimentally in dogs there is an advantage, a theoretical advantage; but practically in the treatment of patients it is not sufficient to warrant the use of a purified protein product. Further, in these individuals we have done amino acid studies and, as far as we can tell from a study of the blood and the amino acid curve after the ingestion of protein, proteins are broken down and absorbed in a normal fashion in these patients. There apparently is no inability, as far as the patient is concerned, to digest and absorb the amino acids of which the proteins are constituted. Knowing that, one would hardly expect much difference between the different proteins as they occur in nature. In the treatment of this particular complex, no one has demonstrated a specific amino acid deficiency, although there has been some evidence that probably cystine might be a little bit lacking in these patients.

DR. EPHRAIM SHORR: Dr. Farr, in the frequently occurring spontaneous improvements in children—that is, when they are not placed on any specific type of diet—do you notice corresponding changes in the plasma protein?

DR. FARR: You mean a child is going along without any change in his regimen and suddenly develops a diuresis and apparently is cured?

DR SHORR: Yes.

DR. FARR: Not necessarily. I have seen diureses occur in these children with a shift in the plasma albumin from 1.1 to 1.3, which is certainly in ordinary parlance not significant, but it is amazing how sharply this critical level is observed by the children, and a very slight deviation on either side will lead to the production of edema or the loss of edema.

DR. SHORR: I wondered whether we might not at the same time think of other factors. One thing that we note clinically is that edema is uncommonly associated with uremia. Wouldn't that possibly point to some influence of the diminished plasma protein on renal excretion itself? That is, may we not consider the renal filtration as taking place under the same circumstances as occurs in filtration of water in the peripheral tissues? So that if you diminish your plasma proteins as you find them diminished, I will say, in nephrosis, you then have a blood with a lowered plasma protein passing through the glomerulus. The decreased osmotic pressure of the proteins is going to offer less resistance to filtration. From the standpoint of the kidney this would seem a very desirable circumstance. This should increase the glomerular filtration and in that way increase the actual renal secretion of urea and all the other metabolites that go with it. It may be that it is that factor rather than a slight shift in the level of the proteins which may bring about the sudden diuresis, when children with nephrosis spontaneously lose their edema.

DR FARR: That is an interesting possibility. In these children the urea clearance will run anywhere from 140 to 300 per cent normal, which indicates an increased renal blood flow. Presumably as the blood goes through the capillary there is an increased capillary filtration due to the reduction in osmotic pressure, but surprisingly enough there also seems to be an increased tubular resorption of water, which more than offsets the increased glomerular filtration, so that the concentration index or the U over B ratio, instead of running around 50 as seen in normal individuals, may go up as high as 100 in these children, which would indicate an excessive concentration of urea in the kidney tubules.

DR. SHORR: So that waste products will be eliminated favorably under these conditions with not necessarily a concomitant elimination of water?

DR. FARR: Water and salt are reabsorbed to an exceedingly great extent.

DR. SHORR: If this increased glomerular filtration as a result of low plasma protein is a factor in human disease, it might be a possible explanation for the observation that patients with edema do not go into the state of nitrogen retention quite as readily as the other type of nephritic?

DR. FARR: What we find is that we can divide these edematous patients into two groups: those with no impairment of nitrogen excreting abilities, and usually their urine nonprotein specific gravity is also normal, and those with an impairment of nitrogen excreting abilities and a reduction in the urea clearance with or without evidence of any nitrogen retention. The reduction of plasma protein does not seem to be the determining factor in inhibiting or enhancing nitrogen retention. In following those patients along, a rapid rise in the serum proteins from a pathologic level with the albumin at about 1 per cent to a normal level with the albumin at about 4 per cent ocurring in a period of three weeks is not accompanied by any demonstrable change in renal function. In acute uremia, particularly that which is terminal, there is such a reduction in the number of functioning glomeruli that it is mechanically impossible

for the body to lose protein as rapidly as it is formed apparently, and the reabsorptive mechanism of the kidney is so seriously impaired that it cannot concentrate the glomerular filtrate to the same extent as it does before that particular phase has been reached. So that in uremia paradoxically enough you often see an improvement in edema accompanied by a loss of electrolytes, and in uremia it is necessary often to give these patients sodium chloride in order to preserve their electrolyte balance. I have seen one girl whose plasma chloride went down to 40 milliequivalents in a terminal uremia, which is less than half the expected normal.

DR. DU BOIS: Dr. Farr, I think a good many of us have noticed that fairly frequently patients given diuretics get a good diuresis and that their general condition becomes much worse following the use of the diuretics. Would you explain that on the same basis?

DR. FARR: Well, it is possible to explain it on the same basis. On the other hand, these patients can show what amounts to a vascular dehydration in the face of edema. That is, apparently they will, even with edema present, show the same response to the lack of fluid as a normal individual. Now apparently in some instances when given diuretics this condition prevails and they have an apparent vascular dehydration with also a loss of extracellular water, which induces an apparent—well I should almost have to call it shock; it is not shock, but that comes the closest to describing it—and by the restoration of fluid volume these patients will often make a spectacular improvement with only a slight increase in their weight and without recovering all the edema that was lost during the diuresis.

DR. DU BOIS: I think the group would appreciate it if you would review some of the contraindications for the use of diuretics. That is a tremendously important clinical question.

DR. FARR: In the treatment of nephritis, one must always be on the lookout for the development of acidosis, and with the development of acidosis of course the acidifying diuretics are definitely contraindicated. In the use of an acidifying diuretic, ammonium chloride, in a nephritic patient, it is desirable, in fact it is almost necessary, to follow the carbon dioxide or chloride to prevent the development of an excessive acidosis with a concomitant uremia. These patients sometimes, even on a small dose of ammonium chloride, will go into uremia in a couple of days, and it is impossible to make a prognostication before the dose has actually been tried as to whether any patient will develop an acidotic uremia under these circumstances or not. If these patients do develop a severe acidosis, discontinue the drug and treat them with alkalis. Mercurial diuretics, I feel, are contraindicated in renal lesions because almost invariably we have found in the administration of the mercurial diuretic, if the urine is carefully examined, that one can find a shower of red blood cells and casts with or without diuresis.

In individuals who have a normal functioning kidney, as in cardiac cases, we have followed the urea clearance after the administration of mercurial diuretics, and curiously enough despite the induction of a most satisfactory diuresis we have often observed an actual fall in the apparent renal function, very consistent in one individual, not great, but always about 10 per cent from the preexisting level, returning to normal within twenty-four to thirty-six hours after the administration of salyrgan or mercurpurin. We feel that since the primary action of these mercurial diuretics is probably on the tubules, and since in the nephrotic syndrome it is the tubule that is most seriously involved, any diuretic which would act on the tubule would be contraindicated.

Our choice of a diuretic in cases of nephritis and nephrosis is urea, and the dose will vary somewhat with the individual. In general we give as much as 40 or 45 Gm. a day even to a 5 year old child, where the urea-excreting mechanism is normal. Where you have impairment of renal function, the dosage of urea should be determined by the elevation of the blood urea nitrogen and an increase of more than 10 to 15 mg. per hundred cubic centimeters should mean a reduction in the dose. The mere elevation of the blood urea nitrogen does not seem to be harmful. I have seen it rise from a value of 16 mg. per hundred cubic centimeters to 82 mg. in a patient by feeding urea without any apparent deleterious effects—no change in the renal function—but we are always a bit hesitant to continue the drug under these circumstances, and certainly the piling up of urea in the blood is to be avoided. When urea increases in the blood to 10 or 15 mg. higher than it was at the beginning of treatment, the maximal diuretic effect that can be obtained with urea is usually present.

DR. HENRY B. RICHARDSON: There was mention of potassium salt. There was some old work tending to show that potassium had an adverse effect on the kidney, wasn't there? It was an old article of Smillie's on that point.

DR. FARR: Potassium and magnesium still are not clear as to their effect on the kidney, whether they are actually deleterious or not; but certainly in these patients where you have—and you always have—an impairment of excretion of these materials, one must be quite circumspect about using potassium or magnesium salts as a diuretic.

DR. HARRY GOLD: Did you ever use thyroid?

DR. FARR: Yes, without any consistent effect.

DR. MILHORAT: May I ask Dr. Farr whether he feels that it is a rational process ever to give amino acids intravenously in any of these cases.

DR. FARR: Amino acids have not been tried in this condition because they have not been available. A preparation that was suitable for intravenous use has certain theoretical advantages and a good many practical disadvantages, but theoreticlly it would seem to be ideal to feed these patients that way when they are unable to take anything by mouth, thus supplementing their diet. We plan to try this.

DR. MILHORAT: May I say a word about the administration of the amino acids? If the technic should be perfected, I think it will be found that the proportions or the relative amounts of the amino acids will be as important as the kinds of amino acid used. In my own work I found that the concomitant administration of a complete protein had no effect on the ability of the animal to utilize gelatin. Blood fibrin is a complete protein, and all the nitrogen is retained by the fasting dog. On the other hand, most of the nitrogen of gelatin, which is an incomplete protein, is excreted. The amino acids in blood fibrin are in such amounts that there are not enough of the nondispensable ones left to make gelatin a complete protein.

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Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

ANTIPNEUMOCOCCIC SERUM, TYPES I AND II COMBINED (See New and Nonofficial Remedies, 1938, p. 399).

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Serum, Refined and Concentrated, Types I and II.—Prepared by immunizing horses with intravenous injections of the virulent and avirulent cultures of type I and type II pneumococci. Trial bleedings are made at frequent intervals, and when the serum has reached a sufficient degree of potency for type I and type II pneumococci the horses are bled aseptically and the serum is refined and concentrated by the method of Lloyd D. Felton (*J. Infect. Dis.*, December 1928, p. 543). The concentrated product contains type I and type II pneumococcus antibodies. After concentration, sterility tests are carried out in the manner prescribed by the National Institute of Health and safety tests are carried out by injection into white mice and guinea pigs. The potency of the product is expressed in terms of the unit described by Felton (*Boston M. & S. J.*, May 15, 1924, p. 819; *J. Infect. Dis.*, September 1925, p. 199; October 1925, p. 309), the unit being $\frac{1}{500}$ cc. for type I and $\frac{1}{150}$ cc. for type II of the control serum (P-11) distributed by the National Institute of Health. Marketed in packages of one syringe containing 10,000 units each of type I and type II, and in packages of one syringe containing 20,000 units each of type I and type II pneumococci, each accompanied by a vial of dilute serum (1:10) for the sensitivity test.

AMYTAL (See New and Nonofficial Remedies, 1938, p. 111).

The following dosage forms have been accepted:

Elixir Amytal, 2 grains per fluidounce: Amytal, approximately 0.44 Gm. per hundred cubic centimeters, in a vehicle containing alcohol 30 per cent, glycerin, water and aromatics; methenamine, 2 grains per fluidounce, is present for the purpose of increasing the solubility of the amytal.

Elixir Amytal, 4 grains per fluidounce: Amytal, approximately 0.88 Gm. per hundred cubic centimeters, in a vehicle containing alcohol 34 per cent, glycerin, water and aromatics; methenamine, 4 grains per fluidounce, is present for the purpose of increasing the solubility of the amytal.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

LIBBY'S HOMOGENIZED BABY FOODS FORMULATED COMBINATIONS NOS. 1, 2, 3, 4, 5 AND 6

Manufacturer.—Libby, McNeill & Libby, Chicago.

Description.—Canned preparations of "homogenized" vegetable, fruit, cereal and soup mixtures, intended for infant feeding or as foods in special diets, available in the following combinations:

1. Peas, beets and asparagus, in equal quantities, with small amounts of added water and salt.

2. Pumpkin, stringless beans and tomatoes (skin and seeds removed), in equal quantities, with small amounts of added water and salt.

3. Carrots, spinach and peas, in equal quantities, with small amounts of added water and salt.

4. Whole milk, whole wheat flour and soya flour, with a small amount of salt.

5. Strained stewed prunes, with small amounts of lemon juice and pineapple juice.

6. Tomato juice, celery, carrots, chicken livers, barley flour and water, slightly seasoned with onion and salt.

Manufacture.—The specified ingredients for each combination are mixed in formula proportions, heated, and a small amount of water added if necessary to furnish the desired consistency. The mixture is then strained in an atmosphere of steam through a stainless steel screen, and the strained mixture is further subdivided or homogenized by being forced through stainless steel valves under 3,500 to 4,500 pounds pressure, after which they are packed in enamel-lined containers and heat processed.

Analyses (submitted by manufacturer).—

	Combination Numbers					
	1	2	3	4	5	6
	%	%	%	%	%	%
Moisture	90.1	92.6	90.6	77.8	67.8	90.2
Total solids	9.9	7.4	9.4	22.2	32.2	9.8
Ash	1.1	0.9	1.0	1.2	0.7	1.1
Fat (ether extract)	0.2	0.2	0.2	1.8	0.6	0.3
Protein (N × 6.25)	2.0	1.1	2.0	5.3	1.1	2.2
Reducing sugars as dextrose after inversion	2.8	2.3	2.1	3.3	17.8	1.9
Crude fiber	0.6	0.9	0.7	0.6	0.6	0.4
Carbohydrates other than crude fiber (by difference)	6.0	4.5	5.5	13.3	29.2	5.8
Calcium (Ca)	0.018	0.024	0.031	0.110	0.027	0.025
Phosphorus (P)	0.056	0.031	0.054	0.151	0.063	0.059
Iron (Fe)	0.0019	0.0014	0.0016	0.0011	0.0075	0.0030
Copper (Cu)	0.0002	0.0002	0.0002	0.0003	0.0005	0.0002
Calories per gram	0.34	0.14	0.33	0.93	1.29	0.33
Calories per ounce	9.7	4.0	9.4	26.4	36.6	9 4

Vitamins.—The firm has provided protocols of biologic assays which show the various combinations to have the following vitamin content:

Vitamin A, U. S. P. units: Per gram—(combination 1) 3.3, (2) 20, (3) 30, (4) 1.8, (5) 7.1, (6) 57; per ounce—(combination 1) 94, (2) 554, (3) 850, (4) 52, (5) 200, (6) 1,630.

Vitamin B_1, international units: Per gram—(combination 1) 0.19, (2) 0.14, (3) 0.19, (4) not reported, (5) 0.16, (6) 0.26; per ounce—(combination 1) 5.5, (2) 4.2, (3) 5.5, (4) not reported, (5) 4.8, (6) 7.5.

Vitamin C (ascorbic acid), milligrams: Per gram—(combination 1) 0.084, (2) 0.056, (3) 0.081, (4) 0.014, (5) 0.106, (6) 0.038; per ounce—(combination 1) 2.40, (2) 1.60, (3) 2.31, (4) 0.40, (5) 3.02, (6) 1.1. International units: Per gram—(combination 1) 1.68, (2) 1.12, (3) 1.63, (4) 0.28, (5) 2.12, (6) 0.76; per ounce—(combination 1) 47.71, (2) 31.81, (3) 46.29, (4) 8, (5) 60.21, (6) 22.

Vitamin G (riboflavin), Bourquin-Sherman units: Per gram—(combination 1) 0.281, (2) 0.147, (3) 0.264, (4) not reported, (5) 0.352, (6) 0.528; per ounce—(combination 1) 8.0, (2) 4.2, (3) 7.5, (4) not reported, (5) 10.0, (6) 15.0.

Claims Recognized by the Council: There is evidence that fruits and vegetables in finely divided form, such as these homogenized foods, are well tolerated by infants as young as 1 or 2 months of age. Because the amounts of iron and vitamin B_1 of the diet of the infant may require more attention than has been given them in the past, some pediatricians may consider that even small amounts of foods containing these nutritional essentials may be a desirable addition to the diet of the young infant. Libby's Homogenized Baby Foods are accepted as foods suitable for use particularly during the early months of infancy.

CLAPP'S CHOPPED PRUNES

Manufacturer.—Harold H. Clapp, Incorporated, Rochester, N. Y.

Description.—Canned chopped prunes, flavored with lemon juice.

Manufacture.—Prunes are pitted, washed and chopped. Lemon juice is added. The mixture is heated in an atmosphere of steam, adjusted to standard consistency, filled into cans, sealed, processed under pressure in steam retorts and cooled.

Analysis (submitted by manufacturer).—Moisture 70.0%, total solids 30.0%, ash 0.7%, fat (ether extract) 1.5%, protein (N × 6.25) 1.1%, crude fiber 2.4%, carbohydrates other than crude fiber (by difference) 24.3%.

Calories.—1.2 per gram; 34 per ounce.

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SATURDAY, MARCH 4, 1939

IODINE BALANCE IN EXOPHTHALMIC GOITER

The discovery by Baumann in 1895 that the thyroid gland of mammals contains iodine in organic combination stimulated other investigators in their attempts to throw light on the true nature of diseases of the thyroid. Two decades after Baumann's observation, Kendall succeeded in isolating the iodine-containing amino acid thyroxine, the active principle of the gland. Elaborate statistical studies point to the interrelationship of the prevalence of goiter in certain localities and the amount of iodine available to inhabitants of these districts. Measures based on this relationship have had widespread influence on public health.

Iodine is an essential component of the thyroid hormone and thus thyroid function and iodine metabolism are intimately related. A recent study of the iodine balance in exophthalmic goiter by Puppel and Curtis [1] is an important contribution to our knowledge of the nature of hyperthyroidism. These investigators realized that the effect of hyperthyroidism on the metabolism of iodine is significant in considerations of disturbed thyroid function. Although hyperiodemia and hyperioduria had been shown in patients with exophthalmic goiter, it remained necessary to study the intake and the excretion of iodine by both normal persons and patients suffering from exophthalmic goiter in order to have a comparative study of iodine metabolism. By carefully controlling the diet, Puppel and Curtis were able to maintain normal subjects on a low intake of iodine. Under these conditions it is found that more iodine is excreted than is taken in; normal persons on a low iodine intake are unable to maintain a positive iodine balance. Persons receiving an average of 29 micrograms of iodine daily lost this element to the extent of 42 micrograms a day. A similar study made on normal subjects during starvation shows that the excretion of iodine in the sweat, feces and urine continues so that an even greater negative balance results. Examination of the iodine excretion of a pregnant woman on a low intake of iodine revealed the fact that the net loss of iodine continued through the eighth month of gestation. A possible explanation of this negative balance in normal persons on a low intake of iodine is that some of the iodine resulting from the breakdown of thyroid hormone is not then available to the thyroid or other tissues and is consequently excreted. Indeed, other investigations indicate that from 163 to 325 micrograms of iodine is utilized daily in the form of thyroxine.

Patients with exophthalmic goiter, maintained on a low intake of iodine, show a negative iodine balance which is from two to three times that observed for normal persons under similar conditions. Although under these conditions the greatest excretion occurs through the urine, the feces are responsible for 40 per cent of the total elimination whereas normal persons maintained on a low iodine intake excrete only 15 per cent in the feces. On an intake of iodine sufficient to keep a normal subject in positive iodine balance, patients with exophthalmic goiter excrete more iodine than they receive and are thus in a negative iodine balance. Feeding of increased amounts of iodine to a normal person previously on a low intake of iodine produces an immediate positive balance. Similar treatment of a patient with hyperthyroidism results in an immediate pronounced retention of iodine and a consequent positive balance which is twice the normal. Patients with exophthalmic goiter show iodine values in the blood which average 9 micrograms per hundred cubic centimeters, in contrast to the value of 4.3 in normal subjects. These data indicate that the increased amount of blood iodine in hyperthyroidism may result from augmentation of total iodine metabolism. There is an increase in its mobilization and an increase in its excretion through one or all of the excretory channels.

These profound changes in iodine metabolism are abolished by thyroidectomy. One patient showed complete recovery from symptoms characteristic of exophthalmic goiter two years and seven months after adequate subtotal thyroidectomy. At this time the iodine balance was normal, although previous to the operation a negative iodine balance had existed despite an adequate intake of iodine. A patient with toxic nodular goiter and hyperthyroidism showed a dramatic fall in excreted iodine to within normal limits as early as the sixth day after thyroidectomy with concomitant clinical improvement. In another case, in which medical management alone brought about clinical improvement, the excretion of iodine decreased and the balance returned to within normal limits.

Although the research by Puppel and Curtis bears directly on the problem of iodine balance in exophthalmic goiter, it also extends our conception of the function of the thyroid gland and has helped further the integration of the various aspects of the problem of thyroid function.

1. Puppel, I. D., and Curtis, G. M.: Iodine Balance in Exophthalmic Goiter, Arch. Path. **26**: 1093 (Dec.) 1938.

EXPERIMENTAL ECLAMPSIA

The recent demonstration by Dill and Erickson [1] of Duke University that a typical eclampsia-like syndrome can be produced in pregnant dogs and rabbits by a simple operation on the kidney suggests a new theory as to the etiology of toxemia of pregnancy and makes possible an intensive laboratory study of the nature and treatment of this disorder. Sheep and guinea pigs occasionally develop eclampsia-like symptoms during gestation. A highly fatal toxemia of pregnancy also occasionally develops in rabbits. Eclampsia in rabbits has been extensively studied by Greene [2] of the Rockefeller Institute, who found that fatalities are not limited to pregnant rabbits but may occur in pseudopregnancy. From this he concluded that the hypothetic toxic factors in this disease cannot arise from the fetus or placenta. Demonstration by Anselmino and Hoffmann [3] that an excess of vasopressin is present in human eclamptic blood led to the hypothesis that the toxic factor in eclampsia is of pituitary origin. This hypothesis is supported by the fact that repeated injections of commercial vasopressin will produce eclampsia-like symptoms and lesions in laboratory animals.[4]

In order to settle these and other controversial questions, Dill and Erickson tested the effects of experimental renal ischemia in pregnant dogs. Nonpregnant females were used as controls. Renal ischemia was produced by the application of Goldblatt adjustable clamps to the renal arteries. Within forty-eight to 120 hours after relatively slight constriction of the renal arteries by this technic the pregnant dogs developed weakness, lassitude and convulsions and exhibited hypertension, hematuria, albuminuria and nitrogen retention. The symptoms deepened to coma, death occurring in from five to fifteen days. Control nonpregnant dogs often failed to show symptoms following mild renal ischemia, hypertension being observed only after the renal clamps had been further tightened.

Following the development of typical eclampsia, two of the Duke University dogs aborted. Rapid improvement and full recovery followed, except for a slight residual arterial hypertension. The significant appearance at autopsy in their eclamptic dogs is practically identical with that described in fatal human eclampsia.

Even more fulminating toxic symptoms were obtained by applying the same renal ischemic technic to pregnant rabbits. Death usually occurred within two to five days, with typical eclamptic lesions of parenchymatous tissues.

The Duke investigators believe that the physiologic and pathologic processes underlying their experimental eclampsia in dogs and rabbits are identical with those of human eclampsia. A study of the presumptive toxic factor is now in progress in their laboratory, in the hope of developing a logical and effective therapy. The only fact definitely established by the Duke investigation, however, is their demonstration that a relatively slight interference with normal renal function is sufficient to cause a fatal toxemia of pregnancy in laboratory animals.

1. Dill, L. V., and Erickson, C. C.: Proc. Soc. Exper. Biol. & Med. **39**: 362 (Nov.) 1938.
2. Greene, H. S. N.: J. Exper. Med. **65**: 809 (June) 1937.
3. Anselmino, K. J., and Hoffmann, Friedrich: Klin. Wchnschr. **10**: 1438 (Aug. 1) 1931.
4. Fauvet, Egon: Klin. Wchnschr. **10**: 2125 (Nov. 14) 1931. Byrom, F. B.: J. Path. & Bact. **45**: 1 (July) 1937.

SIGNIFICANCE OF URINARY AMMONIA

Although the acid-base equilibrium is first maintained by the buffers of the blood and other body fluids, the final removal of acid from the body is effected by the lungs, skin and kidneys. The expired air and the sweat are of peculiar significance as pathways for loss of metabolic acid, as all of the expired carbon dioxide and about half of the lactic acid of the sweat are removed without accompanying loss of base. In the kidney likewise there is a highly important mechanism for the excretion of acid without concomitant loss of fixed base; here it is the formation of ammonia from urea. The formation of this endogenous base in response to the administration of mineral acids was first noted by Walter in 1877. Magnus-Levy, in his classic monograph on diabetic acidosis, called attention to the augmented excretion of ammonia in the urine of such patients and suggested that the level of urinary ammonia might be used as an index of acid excretion. The fact that administration of sodium bicarbonate results in a marked diminution in the production of ammonia by the kidney has served to support further the view that there exists a close relation between acid excretion and formation of ammonia.

A recent statistical study [1] of the correlation between the volume, specific gravity, titratable acidity, p_H and urea nitrogen on a large number of samples of human urine shows a higher coefficient of correlation between ammonia production and titratable acidity than between ammonia and any of the other constituents determined. The lack of definite parallelism between ammonia and p_H was reaffirmed. The exact mechanism or stimulus which brings about the increase of ammonia is not so clear. It has been shown [2] that in the course of fasting the ammonia production is not strictly parallel to the increase in acid excretion but rather inversely proportional to the concentration of fixed base. Again, from a study of the so-called acidosis of pregnancy it was concluded [3] that the elevated urinary ammonia was a sign of decreased level of available fixed base rather than of increased acid excretion. In other words, the formation of ammonia in the kidney is conditioned by the necessity on the part of the body to conserve fixed base. A sign of dissent with this point of view is contained in a recent report by Briggs,[4] who on the basis

1. Cavett, J. W., and Foster, W. C.: Am. J. Physiol. **124**: 66 (Oct.) 1938.
2. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: J. Biol. Chem. **57**: 633 (Oct.) 1923.
3. Oard, H. C., and Peters, J. P.: J. Biol. Chem. **81**: 9 (Jan.) 1929.
4. Briggs, A. P.: Proc. Soc. Exper. Biol. & Med. **38**: 883 (June) 1938.

of failure of prompt adjustment of ammonia to changes in urinary fixed base after forced breathing believes that the function of urinary ammonia is to protect the urinary passages from the acidity of the urine. According to this view it is the acid-base balance of the urine, not of the tissues, which governs the production of ammonia.

The recent studies in which newer experimental procedures have been employed and novel points of view developed have raised questions as to the exciting mechanism of the production of ammonia. The current basic conception has been changed little, if any; the variation in urinary ammonia follows the body's need for the excretion of acid with, at the same time, the maximum conservation of fixed base.

Current Comment

BACTERIOLOGIC INVESTIGATIONS OF PUBLIC HEALTH SERVICE

The bacteriologic investigations of the United States Public Health Service are often overlooked because of the better known activities of this agency in more publicized fields. Most of the original research of the service along these lines was done at the Hygienic Laboratory, the name of which was changed in 1930 to the National Institute of Health. The work of this branch of the service has been recently summarized in a condensed but impressive fashion.[1] Especially noteworthy activities include the control of standards of biologic products for immunization and treatment, important work on disinfectants, especially with regard to fumigation and embalming procedures, and original investigations on encephalitis, leprosy, pellagra, plague, poliomyelitis and rabies, to mention only a few. A continuation of distinguished investigation in these and other fields may be confidently expected.

CLINICAL STUDY OF DRUG ADDICTS

As one part of the extensive studies on drug addiction at the United States Public Health Service Hospital at Lexington, Ky., recently discussed in THE JOURNAL,[1] Pescor [2] presents a statistical analysis of the information contained in the clinical records of more than a thousand admissions. Although addiction may occur at any age, the heaviest concentration of cases occurred in the decade between 20 and 30 and few became addicted after the age of 50. Thus there is greater potential danger of acquiring the habit in youth than in the later years of life. To the question as to why drugs were begun, the most common reply given was "curiosity and association with undesirable companions." Following this in order of frequency was the use of drugs "for the relief of pain or physical distress," "to sober up after alcohol sprees or to relieve hangover" and "relief of fatigue," also as an antidote for environmental distress. Morphine was the first drug used by the majority of patients; opium smoking and the use of heroin followed closely. Although the average period of addiction at the time of admittance was about twelve and a half years, five of the patients admitted addiction of forty years or more and one had used drugs continuously for fifty-nine years. About three fourths of the patients had previously attempted a cure, more than half of these having been enforced, or "jail house," cures. Such "cures" in general did not appear to be as effective as voluntary cures. The educational attainments of the patients were more or less comparable to those of the population at large. The occupational distribution revealed the highest concentration in the personal service classifications and the professional class. The majority of the addicts came from deteriorated and densely populated localities. The tendency to marital failure and inadequacy of social adjustment was strongly manifest. Dental difficulty of a type peculiar to addicts was found in practically every case. The majority of the patients made satisfactory social adjustments before but not after addiction. Finally it was noted that the "voluntary" patients were the least cooperative chiefly because of their insistent demands for release against medical advice.

SENATOR WAGNER INTRODUCES HEALTH PROGRAM LEGISLATION

On February 28 Senator Wagner of New York introduced in the Senate a bill for the carrying out of some of the phases of the National Health Program. In the proposed bill Senator Wagner offers a series of amendments to the Social Security Act calling for an expenditure of federal funds amounting to $80,000,000 the first year with gradual increases over a ten year period for the purpose of establishing, expanding and improving state programs for "(1) child and maternal care; (2) general public health services and investigations; (3) construction of needed hospitals and health centers; (4) general programs of medical care, and (5) insurance against the loss of wages during periods of temporary disability." Senator Wagner said in an interview that it "should be clearly understood that the bill does not establish a system of health insurance or require the states to do so." Funds would be made available under this bill to "those localities and states which are in the greatest need of the services," the size of the grants being determined "on a variable matching basis, depending on the relative financial resources of the several states as determined by the per capita income of their inhabitants." It is not possible at this time to offer a complete analysis of the details of the proposed legislation. Obviously, it will be necessary for suitable committees of the Congress to give careful consideration to the proposals. While the sum announced—namely, $80,000,000 annually—is not large as compared with an annual expenditure of $850,000,000 ultimately proposed by the National Health Program, it represents nevertheless a considerable sum. Senators interested in an economy rather than a spending program have already announced opposition.

1. A Brief History of Bacteriological Investigations of the U. S. Public Health Service, Pub. Health Rep., Supplement 141, 1938.

1. Nine Years of Research on Drug Addiction, editorial, J. A. M. A. **111**: 1846 (Nov. 12) 1938.

2. Pescor, Michael J.: A Statistical Analysis of the Clinical Records of Hospitalized Drug Addicts, Pub. Health Rep., Supplement 143, 1938.

ORGANIZATION SECTION

AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

REPORT OF MIDDLESEX SOUTH DISTRICT (MASS.) MEDICAL SOCIETY, BOSTON

The following report is based on the data recorded on the summary sheet of the Middlesex South District Medical Society. As indicated in the title, the Middlesex South District is not a county but a district society and, as stated in the summary sheet, no estimates of the population in this district can be made. The largest political unit included in this district is the city of Cambridge—a part of the metropolitan district of Boston. Some idea as to the population and economic status of the people in this district may be obtained from the following facts: Harvard University is located in Cambridge, and much of the surrounding area is urban residential districts; there are 169 industrial concerns in Cambridge, of which 143 are manufacturing plants which employ 20,753 workers.

In order to show the number of persons and organizations which contributed the information included in this summary, a list of the number of forms sent out and the number and the percentage of returns is given in table 1.

This table brings out the fact that a larger percentage of the health departments, the welfare and relief agencies, the hospitals, the nurses' organizations and the schools and colleges have contributed data, on which this report is based, than of physicians and pharmacists. Consequently, the statistics in this report are made up primarily of the figures recorded by those organizations. Therefore a summary of the data must present an accurate picture of the supply and need for medical care in this district, since it is not based on the experience of any one group of persons or organizations but on the experience of representatives of all persons who provide medical care and of practically every organization that arranges or furnishes medical care. The public health nurses, the welfare and relief agencies and the health departments are engaged in work that offers them every opportunity to discover persons unable to obtain medical care, so it is very improbable that any lack of medical care could have passed unnoticed by them.

A concise report on the amount of medical and surgical care furnished in 1937 is given in table 2. A study of this table will show that medical care is available to all economic classes, especially the indigent and low-income groups.

Table 2 shows that during 1937 a great deal of medical services, hospitalization, nursing services and medicines were furnished free or at reduced rates to a large number of persons in this area. For the indigent and the low-income group, twenty-three clinics and outpatient departments furnished care at no cost or at reduced rates to persons eligible to receive such care. The colleges provided medical treatment for their students, so they did not need to obtain services from the clinics or outpatient departments. Since we have no figures on the number of persons in this district, it is difficult to determine the adequacy of medical care from the amount of medical care furnished.

From the data given on the lack or need of medical care it is possible to determine more specifically whether some persons were unable to obtain necessary medical care. Three physicians stated that they knew of some persons unable to obtain medical or dental services. The reason for one case was the inability to obtain free dental services. The other cases were due to overcrowding at clinics and inadequate hospital facilities for the poor. Comments from forty-four of the physicians accompanied the report. An analysis of these comments indicated that twenty-two of the physicians felt that there was an opportunity for every one to obtain services at the clinics if they were unable to afford a private physician. Too many of the patients accepted by the clinics could pay for their medical services. Since the physicians devote a portion of their time in furnishing free services at the clinics, either some arrangement should be made to eliminate the patients capable of paying regular fees or physicians should be partially remunerated for their services at the clinics. Three physicians believed that it was the high cost of surgical treatment that caused so many persons with low incomes to feel that they could not afford medical care. Four physicians thought that the most important factor in the lack of medical care among the low-income group was lack of information on the availability of medical care. Two physicians were in favor of compulsory prepayment plans for medical care, or sickness insurance for the low-income group, since this group seemed to be incapable of making provisions to pay for medical care. A few physicians thought that it was the high cost of laboratory tests and x-ray treatments that caused so many people to think that medical care was beyond their ability to pay. To alleviate this condition they recommended free diagnostic centers, maintained by the government.

One hospital reported that 285 patients were refused admittance as bed patients because they were not able to pay for hospitalization. The other sixteen hospitals reported that they had not turned away any patients. The comments from eight hospitals on the methods to improve the supply of medical care may be summarized as follows: There is a great need for a "filter system" that will prevent people who are able to pay for medical care from taking advantage of the free services provided in the outpatient departments and clinics. The local governmental agencies should pay for hospitalization and medical services required by people who are financially unable to pay for such services themselves, after their indigence has been established by a thorough investigation.

The hospital outpatient departments turned away fifty-eight persons because they were not eligible to receive care there. Some were referred to physicians, some to the Veterans' Bureau and the remainder to the eye clinics.

The health departments stated that 15,583 persons in need of medical care were reported to them. These people needed treatment for tonsils, adenoids, teeth, ears and eyes, and orthopedic therapy. It was stated that they were unable to obtain the necessary treat-

ments because there were inadequate free services available. If these people did not receive medical care the responsibility must rest with the local governments, since the health departments had been informed of their need and of their inability to pay for the necessary services. The health departments also reported that 13,585 people had requested medical services from

TABLE 1.—*Distribution of Forms*

	Number Sent	Forms Returned and Used in Study	
		Number	Per Cent
Physicians in active practice*	800	140	17
Hospitals	20	17	85
Nurses' organizations	16	16	100
Health departments	14	12	86
Welfare and relief agencies	13	12	92
Schools	70	64	91
Colleges	6	6	100
Other organizations	..	22	..
Pharmacists	196	46	23

* The information supplied by the dentists in this district is included in the Suffolk district report.

them and that the necessary services could not be obtained for 4,801. The reasons for this inability were not given. Five health departments made statements as to what they considered was needed to meet the need for medical care. Three of the health departments stated that all persons who applied for medical care were getting the necessary care through the cooperation of the public health nurses, the private physicians and the public welfare boards. One health department thought that more clinics for tonsil and eye cases were needed. Another stated that outside of the communicable diseases, for which adequate care was provided, they had no information on need for medical care.

The welfare and relief agencies reported that they knew of no persons who needed medical care that could not obtain the necessary care. If the 20,384 persons reported by the health departments as unable to obtain medical, dental, hospital or nursing services were referred to the welfare and relief agencies or the public health nurses, then they evidently received the necessary services since the welfare and relief agencies and the nurses stated that they were able to arrange or provide medical services in every instance in which they found a need for such services. There appears to be a lack of cooperation and agreement between the health departments and the welfare and relief agencies and public health nurses in this area. The comments from the welfare and relief agencies indicated, however, that the people they dealt with might not be furnished with all the medical care they needed. They stated that they lacked funds to provide dental care, eye examinations and glasses to some of their clients. They also believed that many people with low incomes waited too long before obtaining necessary medical or dental care but, in their experiences, they knew of no cases in which medical or dental care could not be obtained if requested.

The public health nurses reported that they had not found any person in need of medical care who could not be furnished with the necessary care. The general experience of the nurses, as stated in their comments, was that they occasionally found a person in need of medical treatment who had made no attempt to obtain such treatment because he felt that he could not afford the cost. In such cases the nurses experienced no difficulty in furnishing medical care. The nurses have always found the private physicians and the welfare and relief agencies willing to cooperate with them in their work. To the nurses the big problem is economic—not medical—since so many people have such low wages that they are unable to maintain a standard of living that is conducive to good health. These same people are not eligible for governmental aid in obtaining necessary goods and services, which they need as much as the totally indigent persons who are cared for through the use of government funds.

In the elementary or secondary schools the examinations provided by the school boards revealed that 19,237 pupils were in need of medical or dental care in 1937. Of this number 2,000 were unable to obtain the recommended care because their parents were unable to pay for it or because there were not enough free clinics where the treatment could be obtained. The comments from the schools were, in general, that the parents cooperated very well with the recommendations of the school physicians, although there was some difficulty in obtaining glasses and dental care for many of the children whose parents lacked the funds to pay for such services and items themselves.

The colleges and universities provided their students with the necessary medical care through their infirmaries and staff of physicians.

TABLE 2.—*The Amount of Medical Care Furnished in 1937 According to the Persons and Organizations That Provided It*

	No.	No. of Beds	Pay and Part Pay Patients	Public Charges	Free Patients
Hospitals	17	2,979	33,355	3,771	3,929
Patient days	..	.....	417,094	58,236	53,863
	No.	Total Number of Patients		Total Number of Visits	
Outpatient departments and clinics	9	24,434		61,324	
	No.	Total Number of Visits		Percentage of Visits Made Without Charge	
Public health nurses	51	84,471		30.5	
	No.	No. of Free Prescriptions		No. of Prescriptions Provided at Cost or Reduced Rates	
Pharmacists	46	2,810		6,870	
	No.	Total Number of Persons Who Received Free Care in Home or Office		Total Number of Hours Devoted to Care of Free Cases in Clinics	
Physicians	140	16,090		27,881	
Per physician		115		199	
					Number
Clinics maintained by the health department					11
Clinics maintained by welfare and relief agencies					3
Schools which have health supervision					64
Colleges which have health examination and supervision					5

The number of free prescriptions furnished by the pharmacists has been given in table 2. The pharmacists' ideas on the methods of supplying medical care is presented in the following summary of their comments. The public is well supplied with medical care and the physicians and the pharmacists have contributed more than their share of free services and medicine in making this care available to the poor. The local governments should apportion funds to be used to pay for medicine prescribed by the physicians to patients who are in the low-income class, as well a for the indi-

gent. The indigent should have the privilege of calling their own physician and of obtaining prescribed medicine at their local pharmacy.

The study on the supply of medical services in industrial plants was made with the aid of Mr. Winthrop Taft of the Harvard Business School, who was employed to collect the data and information from the 169 industrial concerns in this district. This group is made up of 143 manufacturing plants, and the remaining twenty-six are warehouses, banks and small stores.

The 143 manufacturing plants employ 20,753 persons. Of this number 51 per cent of the workers receive some medical attention through their employment, but only seventeen of the 143 plants have the services of a physician available or on call. Nursing services are available in twenty-one plants, which includes 64 per cent of the 20,753 workers. Seven of the plants require annual physical examinations, and eighteen plants give physical examinations when the workers are hired. Forty-four plants, employing 82 per cent of the total workers, maintain first aid rooms, but there is one plant employing 200 people that does not provide even a first aid kit, although the law requires that all plants employing 100 persons or more must provide first aid rooms. The amount of medical care provided by the twenty-six warehouses, banks and stores is negligible, as no establishment employs as many as 100 persons.

The following recommendations concluded the report on medical care in industrial concerns:

It is recommended that:

1. Medical supervision of plant employees be increased.
2. Annual physical examinations be increased.
3. Health records be increased.
4. Cambridge physicians be used more extensively (in order that a doctor would have personal interest in a plant rather than being representative from an insurance company or hospital).
5. More dental clinics be fostered in the community where dental care can be given within the patient's means.
6. Health education be increased.

The members of the Middlesex South District Medical Society's Committee on the American Medical Association's Study of the Need and Supply of Medical Care made an appraisal of the comments submitted by the physicians and pharmacists concerning the need of medical care and the methods that they believed should be considered in meeting this need. Because this committee is more qualified to interpret and explain the comments of the local physicians and pharmacists, its report is printed below:

There is little doubt in regard to the unanimous attitude of the doctors that they are making every reasonable attempt to provide medical care for all who need it. This desire, however, is tempered as well as at times tried because of certain disturbing conditions. The first of these is the obvious attempt on the part of some to secure medical attention gratis when a reasonable fee could be paid. The matter, however, is not simply that of trying to distinguish patients on the basis of minimum financial ability. Other things enter the picture. For example, a number of doctors have commented on the expense of laboratory, x-ray and other special services needed for diagnosis. The expense of these seems at times to be out of proportion to the small income of the patient, since such services increase substantially the total cost to the patient. Even more serious is the public relations aspect as indicated by the comment "I observe that clinic patients can obtain laboratory and x-rays for a lower price than private patients that I send to hospitals for this work. This discourages the pay patients to come to me and many go directly to clinics the next time they require such work. I believe that a set price should be established for such work." Other comments seem also to point toward a potential case of carelessness with which the social services may be charged when deciding, without careful inquiry, to send patients where they may obtain free advice.

Another comment made by many physicians is that the very poor have far better medical assistance than those wage earners whose incomes are in the lower brackets. Often these patients have to bear the full cost of medical care simply because they are receiving a nominal income. This serious problem appears to revolve about the question of how in an economically and socially wise manner medical care may be provided for these people. Some of the replies reflect a hasty opinion that the government might as well provide the cost of this service, implying that the government has already wasted more than enough to cover all such needed help to the citizens. This position, however, appears to beg the question, since there are many individuals who are either too proud to come or who because of a technical fact of small income cannot come under this government control. The doctors making the comment of "let the government do it" appear to forget that such a move on the part of the government represents a first step toward full government control of medical services to the whole population.

A number of the comments reflect the well known fact that in many instances the less well-to-do and the poor are as inefficient in caring for their health as they are in their economic position. Lifting an individual out of trouble with regard to his or her ailment consequently does not lead necessarily to a permanent cure.

On the other side of the picture there is the question of how much time, energy and also out-of-pocket expense the doctors should be expected to provide. Many of the comments reflect the ever present struggle to earn a living. The thought that this might be avoided through some kind of sovietized medicine recalls once more the dread of politics and lowered standards.

Turning now from the point of view of the doctors to that of the pharmacists, we find some interesting suggestions. These concern the patients from the lower economic classes. The pharmacists comment that the socially poor tend to ask for medical care in the case of trivial ailments. This observation is coordinate with that of the doctors, indicating that the fundamental trouble with many of these people is a poverty in understanding and wisdom as well as that of pocketbook and social position. Also, in the minds of the pharmacists, many clinics are too hurried for full diagnosis.

There is no doubt that the pharmacists are anxious to cooperate with the doctors. The service, however, which they render to indigent and low income groups of customers is given more from a feeling of business charity than is true of the gratis service of doctors which originates in knowledge that they are following a profession.

There is apparently the serious difficulty of fee and public payment plan between politicians, doctors and pharmacists in the case of some charity patients. This would lead one to inquire whether for the poorer patients the whole relationship between doctors, patients and pharmacists, with the politician on the side, ought

not to be reviewed very carefully by physicians in order that they might fully understand one phase of public relations in public health work.

With reference to the special instances, one pharmacist indicated that the physicians whose prescriptions he fills are not always too thoughtful regarding the expense of the drugs prescribed. This pharmacist comments "After forty years in the business I am convinced that the patient is asked to pay too much for specialty prescriptions. The physician writes for some specialty either not knowing the cost or at least not telling the patient, and the result is that the patient thinks he is being robbed."

In summary it may be said that both doctors and pharmacists are vitally interested in the health of the community from the point of view of a wholly sound and highly professional attitude. This is well known. There appears to be in the situation, however, some difficult problems. These center about the means of providing medical care for the lower income groups and surgical care for the very poor according to some plan which will provide the attending physician with a financial return sufficient to enable him to maintain self respect among his fellows. There is, in addition, the serious problem of coordination between doctors and pharmacists. Possibly doctors have been too inclined to take the pharmacists for granted and too ignorant of the business side of the drug store. Finally, the comments in many instances hint at unsolved problems of human relations. These problems should be discovered, their causes disclosed and their cure begun. Only in this way can the medical profession through its own activity avoid what is believed to be the very bad alternative of governmental control.

THE COMMONWEALTH FUND AND EXTENSION TEACHING

Abridgment of Report on Postgraduate Study and Extension Teaching from the 1938 Annual Report of the Commonwealth Fund, New York City.

The Commonwealth Fund encourages postgraduate study in several ways: by giving fellowships for study at selected medical schools to physicians in certain parts of the country through the Divisions of Rural Hospitals and Public Health, by subsidizing the development of university facilities for postgraduate teaching and by joining with state medical societies and health authorities in setting up extension courses which take instruction to the doctor in his own bailiwick.

Whatever the content, the division believes that postgraduate study is rewarding if it brings the student into close personal touch with an outstanding and modern-minded teacher—discipleship plays a large part in medical education—if it helps him to make the best use of books and journals, and if it gives him a sound approach to diagnosis.

In the public health program, emphasis falls on general brush-up courses for physicians practicing in the states in which the fund is subsidizing public health work, and in some instances in neighboring states. To meet the preferences of such men, the four month courses hitherto offered at Vanderbilt have been broken up into four units of a month each, to be taken separately at the physician's convenience. It is understood, however, that the month in physical diagnosis and internal medicine is to come first and is to serve as a foundation for the courses in surgical diagnosis, obstetrics and pediatrics. A similar arrangement is in force at Harvard for postgraduate students from the four northern New England states.

Postgraduate teaching under university auspices may be done either on the campus or in the field. On the initiative of its late president, L. D. Coffman, the University of Minnesota recently found a fresh way to lure busy men and women back to the campus. A building was put up for their special use, and a schedule of week-long courses in many fields keeps this dormitory-teaching center in constant use. All the circumstances favor serious and concentrated work. Courses in medicine form an essential part of the plan; physicians enrolled readily for the first of these courses and in some instances came back again and again for more. The fund has made it possible for the university to employ a full-time director to develop these medical courses to their fullest possibilities.

At Tulane University, where resident postgraduate medical instruction is of long standing, the fund has helped to set up a division of extension education which, in collaboration with various professional agencies, offers instruction in the field. This division has arranged courses in pediatrics and syphilology which have already reached several hundred physicians in Mississippi. Here the unit of instruction is a series of lectures every day for a week, but some of the best teaching is done by the instructor in consultation with individual physicians outside the regular sessions. The state medical association and the state department of health in Alabama have now joined in asking that similar courses in internal medicine be offered in that state.

Meanwhile, field instruction in obstetrics, following the pattern used with such success in Virginia and Mississippi, has been continued for a second year in Tennessee with a full-time instructor employed jointly by the state medical association, the state health department, the two medical schools and the Commonwealth Fund, and a similar arrangement was launched during the year in Oklahoma. Both projects have been highly successful. Something over 1,100 physicians have been enrolled in Tennessee, and the initial response in Oklahoma surpassed all expectations. In one circuit, in rough, hilly country in Oklahoma, a doctor distinguished himself by driving eighty miles from his home to the nearest center of instruction to make up for a session which he had been forced to miss because of an emergency call.

The scholarship plan by which the fund seeks to steer promising medical students into rural practice has now carried thirty-three young men through medical school and into small-town offices, with seventy-eight more on the way.

Medical education underlies the fund's field programs in public health, rural hospitals and mental hygiene. When the sums earmarked for this purpose are brought together from the budgets of these programs and added to those appropriated directly in the form of special grants, they total, for the year just ended, approximately $375,000.

GRADUATE MEDICAL EDUCATION

A PROGRESS REPORT OF THE FIELD STUDY ON GRADUATE MEDICAL EDUCATION IN THE UNITED STATES BEING CONDUCTED BY THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

OKLAHOMA

In 1925 the director of the Extension Division of the University of Oklahoma adapted North Carolina's plan for continuing the training of practicing physicians to the needs of Oklahoma. The dean of the University of Oklahoma School of Medicine became interested and was appointed the first chairman of a committee of three, with the superintendent of the university hospital and the professor of internal medicine of the school of medicine as members. The director of the extension division served as an ex officio member. A budget of $1,500 was appropriated by the president of the university, although it was proposed that the extension programs be self supporting. A field director was appointed and an out of state pediatrician who was experienced in conducting graduate courses on a circuit basis was engaged. County medical societies throughout the state were presented with the plan and voted on its acceptance. Six circuits of seven centers each were set up the first year, and within fourteen months the state was covered, and slightly more than 1,100 physicians had subscribed for the series of twelve lectures. A registration fee of $30 was charged.

The extension division of the university continued to administer the graduate program, publicize the courses and organize the instructors' itineraries. Physicians who gave the instruction were engaged by the university. The extension division later provided for the financing, prepared the announcements and arranged for enrolment of practicing physicians.

In 1926 other courses were given in internal medicine, a series of nine lectures with clinics and consultations in seven teaching centers.

The course in internal medicine was repeated in 1927 with another guest lecturer, who gave three hours of lectures and clinics weekly for nine or ten times. An organizer from the university's extension division assisted each county society which elected the program. The fee for this series was $35. A short course in the examination, diagnosis and treatment of tuberculosis was arranged in each of the three state tuberculosis sanatoriums. Illustrated lectures, laboratory demonstrations and clinics were given by the hospital personnel for one week. Each class was limited to twenty physicians; the fee was $7.50. Demonstrations and lectures in physical therapy were conducted for one week at the medical school by an out of state physician, with the use of the facilities of the university hospital.

In 1928 one week intramural courses in surgical diagnosis and in medical diagnosis were held in Oklahoma City, while the instruction in tuberculosis was repeated in one of the state sanatoriums and courses in physical therapy and surgical diagnosis were given in Tulsa.

Intramural courses designed for practicing physicians were given in obstetrics, gynecology, pediatrics, urology and eye, ear, nose and throat during 1929. Five or six out of state specialists constituted the faculty for the week of instruction in each subject. The enrolment for each course was limited to forty physicians. Fees were $35. In addition the extramural course in internal medicine was repeated in six teaching centers of the state.

The graduate activities of the first five years resulted in a deficit greater than the university could assume. The Oklahoma State Medical Association therefore donated approximately $700 in order that the field director might continue his work. Full time instructors were discontinued and teams of three prominent guest speakers were invited to visit the state for a week's period. Each of these instructors gave six lectures to any county medical society that would pay the traveling expenses. Attendance varied at these meetings from twenty-five to 250 physicians, depending on the number of physicians practicing in the sections visited.

In 1929 officers of the state medical association proposed to the extension division of the university that medical and surgical motion picture films be distributed among the county medical societies of the state. Approved films were purchased by the state association; the extension division serviced them, arranged for booking and distributed them to various county societies. The only charge to the local societies was for transportation of films to and from the university. When local operators were not available, they were provided for a small fee. The films were widely used throughout the state and at the University of Oklahoma School of Medicine. In 1933 films were shown in seventy-seven towns and in all but two cases were without expense to the state medical association.

During the period 1929-1930 the University of Oklahoma provided the otolaryngologists and ophthalmologists in two centers of the state with one week of instruction, including pathologic anatomy with material for dissection. Again prominent teachers visited the state and supervised dissections. Two graduate physicians were assigned to each cadaver. University hospitals provided facilities. A fee of $50 was charged, thus providing competent instruction. Groups of from twenty to sixty physicians enrolled and the venture proved successful financially.

From 1930 to 1933 the practicing physicians of the state were again provided with prominent out of state instructors, who gave intensive intramural courses at Oklahoma City and one circuit course throughout the state. In 1931 there were an intramural course and a series of circuit courses which were held in six centers of the state. In 1932 two courses were given in each of the eleven centers as well as one intramural program on degenerative disease.

The state medical association appropriated sufficient funds in 1933 for four courses of instruction, one each in obstetrics and gynecology, in surgical diagnosis, in traumatic surgery and in degenerative disease. Thirty-six out of state speakers participated in these courses, which were given in twenty-six centers of the state. Twenty-eight in state physicians also participated. Cancer teaching clinics were organized in several parts of the state and were attended by 1,137 physicians.

There were approximately 1,900 physicians who received instruction in one or more of the subjects given during 1933. The state medical association spent $700, the state of Oklahoma appropriated $1,431 and the physicians paid fees totaling $5,065. The deficit was made up by the extension division of the university.

The courses were discontinued at this point because the governor of Oklahoma withdrew financial support from the extension division of the university. In addition, cultists attempted to gain entry to the state courses in October 1933, and three years passed before it was possible to resume the graduate program which had had such an auspicious beginning.

At this time a joint committee composed of representatives from the state medical association and the faculty of the school of medicine developed a speakers' bureau. The university extension division issued a bulletin containing the names of 100 Oklahoma physicians and the subjects on which they would speak. The secretary of every county medical society was provided with a copy so that some graduate training might be continued to this extent.

In 1936 the state association's special committee on postgraduate medical teaching again planned an extensive program of graduate instruction. The committee was composed of three members with Dr. Henry H. Turner as chairman. Three out of state speakers were engaged to give courses in cities in the western half of the state. Subjects of general interest to practicing physicians were included at this time.

In 1937 the request of the postgraduate committee of the state medical association for an appropriation of $2,000 was granted in order that a state wide postgraduate program in obstetrics might be financed. The Commonwealth Fund of New York made a very substantial contribution and the Oklahoma Health Department also assisted financially. Under the plan ten lectures, clinics and demonstrations in obstetrics would be given at weekly intervals in county seat towns or centers where physicians customarily met for county medical society meetings. A full time instructor was engaged and a field director familiar with the state employed to make the preliminary arrangements. The plan is similar to the one which operated so successfully in Tennessee.[1]

1. Graduate Medical Education: Tennessee, J. A. M. A. **111**: 725 (Aug. 20) 1938.

The state was divided into nine teaching circuits. Five cities in each circuit were selected as teaching centers. The first course began on April 4, 1938, in the northeastern part of the state. By November 15 three circuits had been completed and 244 physicians in thirty-one counties had received instruction. Enrolment for the fourth circuit totaled 115. It is expected that the nine circuits in the state will be covered by January 1940.

In each teaching center a clinic chairman arranges for clinics and for consultations whenever the latter are requested by local physicians. A record of attendance is kept. The registration fee is $5 for the series of clinics, which include manikin demonstrations. The fact that the success of the clinic depends largely on the cooperation of physicians in the community makes the program a responsibility of the local profession, thus assuring keen local interest. A minimum of fifteen physicians must register in a center before a course may be given.

In addition to practicing physicians attending obstetric lectures and clinics, nurses who assist local physicians are invited to listen to the instruction. Superintendent nurses of obstetric hospital wards are invited also, as well as nurses employed full time by county health units. No fee is charged nurses for this training, since the course is arranged primarily for physicians.

The committee on postgraduate medical teaching has an advisory committee of six members with the commissioner of health of the Oklahoma Health Department and the dean of the medical school as members. The health department has cooperated by rendering financial assistance. Mimeographed notes of the lecturers are prepared by the committee's secretary. These are bound and distributed to physicians on completion of the course. The medical school has contributed equipment which is used in illustrating the lectures. It is estimated that the total expenditure for this type of instruction will approximate $19,500 to provide for the salary and traveling expenses of the clinical instructor and field director and the salary of a full time office secretary, in addition to miscellaneous expenses for supplies and equipment. The treasurer of the state medical association disburses the funds on the approval of vouchers by the committee chairman.

The Oklahoma Health Department began a series of postgraduate courses in venereal disease in October 1938. These courses are given one day each week for five times without cost to physicians. They are conducted by a member of the health department and will be given until the entire state is covered. The president and secretary of each county medical society are notified when lectures are to be held and are responsible for making the local arrangements. Instruction is limited to practicing physicians only. Thus far, four counties have been visited and 157 physicians in these areas have attended the lectures.

The Oklahoma City Clinic sponsored by the Oklahoma City Clinical Society has been given each year since 1930 by a group of physicians in the Oklahoma County Medical Society. The clinical society consists of 150 members of the 290 in the county medical society, each member contributing $10 a year. This organization brings to Oklahoma City sixteen prominent guest speakers, who are given traveling expenses only. The meetings are of four days' duration and consist of a series of lectures and round table discussions, which are held in a local hotel. The director of clinics, at present Dr. Wendell Long, has charge of local arrangements. Commercial exhibits, thirty in number, aid in financing the clinical conference. The number of physicians who have registered has increased from 385 in 1933 to 522 in 1937. Approximately 80 per cent of those who attend are from Oklahoma and the remainder are distributed throughout the ten states in this section of the country. Registration fees are $10. The conferences are announced in state medical journals and by letter to approximately 13,000 physicians.

The Commonwealth Fund of New York offers eight scholarships each year to practicing physicians of Oklahoma who desire to spend three or four months of graduate study in a medical center. Each applicant is interviewed by a member of the staff of the Commonwealth Fund. Physicians who are selected are given a small stipend and are provided with traveling expenses and tuition. This plan, which has operated so successfully in other states, was begun in Oklahoma in 1938.

There are 2,364 physicians in Oklahoma, 1,457 of whom are members of the Oklahoma State Medical Association.

OFFICIAL NOTES

ADDRESSES BY OFFICIAL STAFF

DR. PAUL C. BARTON:

March 8—Interprofessional Relationship Committee of the Hennepin County Medical Society, Minneapolis.

DR. W. W. BAUER:

March 6—Woman's Club, People's Church, Chicago.
March 13—Marquette University, Milwaukee.
March 20—Men's Civic Club, Antioch, Ill.
March 21—Young Women's Club, Bryn Mawr Church, Chicago.

DR. MORRIS FISHBEIN:

March 6—Southeastern Surgical Congress, Atlanta, Ga.
March 7—Executives' Club, Charlotte, N. C.
March 13—Lay audience, auspices Payne County Medical Society, Stillwater, Okla.
March 13—Banquet, Payne County Medical Society, Stillwater, Okla.
March 14—Three civic clubs, Shawnee, Okla.
March 14—Pottawatomie County Medical Society, Shawnee, Okla.
March 15—Jackson County Health Forum, Kansas City, Mo.
March 17—Northwest Branch Chicago Medical Society, Chicago.
March 22—Phi Beta Lecture, Mercy Hospital, Chicago.
March 23—Chamber of Commerce, Lions and Rotary Club, Hannibal, Mo.
March 23—Marion-Ralls County Medical Society, Hannibal, Mo.
March 29—St. Joseph Clinical Society, St. Joseph, Mo.
March 29—Public meeting, auspices St. Joseph Clinical Society, St. Joseph, Mo.

DR. PAUL A. TESCHNER:

March 9—Public school, Cicero, Ill.
March 10—Woman's Auxiliary, Milwaukee County Medical Society, Milwaukee.

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-four weeks. The program is broadcast each Wednesday over the blue network of the National Broadcasting Company at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).[1]

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

March 8. Water, Waste and Sanitation.
March 15. Guarding Fresh Foods.
March 22. Auditing the Health Record.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Bills Introduced.—S. 1383, introduced by Senator Brown, Michigan, and H. R. 4496, introduced by Representative Lesinski, Michigan, propose that no citizen of any foreign country the boundaries of which touch the boundaries of the United States shall be permitted habitually to cross the international boundary line for the purpose of seeking employment or engaging in any employment, vocation or trade in the United States. S. 1557, introduced by Senator Shipstead, Minnesota, proposes to enact a National Epilepsy Research Act. This bill proposes to create in the United States Public Health Service a National Epilepsy Institute to conduct researches, investigations, experiments and studies relating to the cause, diagnosis and treatment of epilepsy; to assist and foster similar research activities by other agencies, public and private; and to promote the coordination of all such researches and activities and the useful application of their results, with a view to the development and prompt widespread use of the most effective methods of prevention, diagnosis and treatment of epilepsy. This bill is modeled closely after the National Cancer Institute Act. S. 1563, introduced (by request) by Senator Andrews, Florida, proposes to provide payment of pensions and increase in pensions to all veterans in all wars, their widows and dependents and certain peacetime soldiers. The word "veteran" is defined in the bill in such a way as to exclude contract surgeons of the Spanish-American War. H. R. 4421 and H. R. 4422, introduced by Representative Bloom, New York, propose, respectively, to establish a chiropody corps in the Medical Departments of the Navy and Army. H. R. 4425, introduced by Representative Cochran, Missouri, proposes to provide for reorganizing agencies of the government. The bill does not provide for the creation of a federal department of health nor will the establishment of such a department be possible under the provisions of the bill if it is enacted. H. R. 4427, introduced by Representative Green, Florida, proposes to authorize an appropriation of $1,550,000 to construct a marine hospital in Florida on a site to be selected by the Federal Board of Hospitalization.

STATE MEDICAL LEGISLATION

Alabama

Bills Introduced.—S. 115 proposes to require a physician diagnosing or treating a case of syphilis, gonorrhea, chancroid, lymphogranuloma inguinale or granuloma venereum to report the facts immediately in writing to the county health officer. S. 116 proposes to authorize a county health officer (1) to require all persons infected with a venereal disease to undergo treatment therefor and (2) to isolate or quarantine persons infected with venereal disease and to commit to jail for treatment persons refusing to take or continue treatments.

Arizona

Bills Introduced.—H. 209 proposes to require every physician or other person engaged in the prenatal care of a pregnant woman, or attending her at delivery, to obtain a specimen of her blood not less than ten days after the first professional visit and to submit that sample to an approved laboratory for a standard laboratory test for syphilis. S. 165, to amend the naturopathic practice act, proposes to authorize the issuance without examination of a license to practice naturopathy to any person who has practiced naturopathy in the state for at least three years prior to January 1, 1939, provided application is made within sixty days after the date this bill becomes a law and is accompanied by a fee of seventy-five dollars. H. 249 proposes (1) apparently to repeal all existing law with respect to the practice of the healing arts, (2) to create a board of examiners in the healing arts and (3) to prohibit the practice of any branch of the healing arts unless licensed by this board. The board in the healing arts is to consist of one doctor of medicine, one osteopath, one chiropractor and one naturopath. The bill proposes that any person practicing more than one branch of healing is to be required to obtain a certificate of license for each branch so practiced. The bill then attempts to define the practice of medicine, the practice of osteopathy, the practice of naturopathy and the practice of chiropractic. The practice of medicine is defined "as a system of treating the abnormalities of the human mind and body by all forms of materia-medica and surgery." Naturopathy is defined as "a system of treating the abnormalities of the human mind and body by all forms of physiotherapy including the use of physical, electrical, hygienic and sanitary measures incident thereto, and does not include materia-medica or surgery." It would seem, therefore, that a doctor of medicine would be limited by a license to practice medicine to the use of "all forms of materia-medica and surgery," and that if he desired to use any form of physiotherapy it would be necessary for him to be licensed also to practice naturopathy. The bill proposes to permit all licentiates to use the title of doctor or physician, to give all licentiates equal rights and privileges in all city, county and state institutions, agencies, institutions or hospitals deriving any support from the public funds and to give them equal rights and privileges under the workmen's compensation act and all health laws.

Arkansas

Bills Introduced.—S. 242 proposes to exempt from the payment of any privilege or occupation tax levied by any city or town which does not maintain a free medical clinic any physician whose services are largely given to the care of the indigent sick. S. 308 proposes that when any state agency empowered to issue or revoke any license refuses to issue or revokes a license the agency must make a report, setting forth the grounds for its action and, on request of the aggrieved person, must transmit the record to the appropriate chancery court. H. 366 proposes to create a state hospital board to be composed of the secretaries of the Medical Examining Board of the Arkansas Medical Society, the Eclectic Medical Examining Board, the Homeopathic Medical Examining Board, the Osteopathic Examining Board and the Chiropractic Examining Board. This board is to require the registration of every hospital in the state and is to charge each hospital an annual registration fee of not more than $5.

Bill Passed.—S. 304 passed the senate February 21, proposing to classify as an investment company a person or organization issuing any form of contract or certificate to furnish hospitalization and/or medical care at a future date and to require such persons and organizations to obtain a permit from the Securities Division of the Bank Commission to file reports, to submit to examination and to pay similar fees therefor as is now required by law of all other investment companies.

California

Bills Introduced.—A. 2112 proposes to create a State Board of Eugenics, which is to be authorized, on the application of the superintendent or warden of any state institution, to order the sexual sterilization of particular inmates of state institutions. Apparently sterilization may be ordered when any inmate, if released without sterilization, would be likely to procreate a child or children who would have a tendency to serious physical, mental or nervous disease or deficiency. A. 2338 proposes to create seven crippled-children hospital districts in the state, each district to provide special care and treatment, transportation and physical rehabilitation for physically defective and handicapped persons under the age of 18. A. 2494 and A. 2501 proposes to authorize the organization of corporations to write insurance against the need for medical and hospital services. The bill apparently contemplates that a company so organized may provide medical services through licensed physicians in its employ. A. 2585, to supplement the Business and Professions Code, proposes to enact a massage, electro-physio-hydro-therapy practice act and to create a state board to examine and license persons applying for such licenses. Apparently licentiates of the board are to receive one of two types of licenses: (1) a license to practice suggestive therapy, physiotherapy or magnetic healing and (2) a license to practice massage, Swedish movements, medical gymnastics, and electro, hydro, vibro, helio, thermo, zone or mechano therapy. The bill

defines physio-therapy as the "treatment by mental impression or suggestion." A. 2764, to amend the provisions of the Business and Professions Code relating to ophthalmia neonatorum, proposes that it is to be the duty of the attending physician where a child develops ophthalmia neonatorum within two weeks after birth to administer silver nitrate and to report the case within twenty-four hours after knowledge to the appropriate local health officer. A. 2745, to supplement the Business and Professions Code, proposes to permit any person whose license has been revoked to file an action in the superior court in the county in which he resides to determine all questions of law and fact pertaining to the revocation and to give that court full jurisdiction in the matter, provided that action is instituted in that court within sixty days after revocation of the license. A. 2436, to amend the law approved May 3, 1933, requiring the use of materials and supplies substantially produced in the United States in public works and for public purposes, proposes that the act shall not apply to medical and surgical instruments, scientific equipment, microscopes, lenses, or instruments used for scientific or medical research.

Colorado

Bill Introduced.—S. 332 proposes to restrict licensure in medicine, chiropractic, chiropody, mid-wifery or any of the healing arts to citizens of the United States.

Connecticut

Bills Introduced.—S. 290 proposes to prohibit any hospital receiving a state appropriation from requiring or permitting any female nurse to work more than eight hours in any one day, nor more than forty-four hours in any one week. H. 464 proposes to amend section 3 of the charter of the Connecticut State Medical Society so as to provide that the house of delegates shall be composed of (1) the president, president-elect, treasurer and secretary; (2) delegates to be elected annually by the several county medical associations; and (3) eight councilors to be elected from time to time as provided in the charter. H. 845 proposes to create stated persons a body politic and incorporate by the name of The College of Natureopathic Physicians. The corporation's object is to be instruction in the principles, practice and theory of naturopathy and the corporation is to have the right to establish and maintain hospitals, sanatoriums, infirmaries and clinics and to award the degree of Doctor of Natureopathy to such persons as it deems entitled thereto. H. 1009, to amend the medical practice act, proposes apparently to provide for an eclectic medical examining board. H. 1025 proposes to make it an offense punishable by a fine of not less than $500 for any institution receiving state aid to interfere or attempt to interfere with a patient in determining what physician shall attend him within the institution.

Delaware

Bill Passed.—S. 27 passed the Senate February 23, proposing to require every physician attending a pregnant woman to take or cause to be taken a sample of her blood at the time of the first examination and to submit that sample to an approved laboratory for a standard serologic test for syphilis.

Bill Introduced.—S. 57 proposes to repeal the laws relating to the Delaware Commission for the Feeble Minded and to create a Delaware Commission for the Mentally Deficient, which is to have jurisdiction and control over the Home for the Mentally Deficient.

Georgia

Bills Introduced.—S. 139, to amend the osteopathic practice act, proposes to require an applicant to be a graduate of an accredited high school, to have completed not less than two years of college work "according to the Carnegie units, in an approved college of arts and sciences," and to have obtained a diploma from some legally incorporated and reputable school of osteopathy requiring a course of study of not less than four terms of nine months each. Apparently the present osteopathic practice act imposes no educational qualification other than graduation from an osteopathic school requiring a course of study of at least three terms of nine months each. H. 399, to supplement the workmen's compensation act, proposes to make compensable disability arising from some twenty-five stated occupational diseases.

Idaho

Bills Introduced.—S. 144, to amend the osteopathic practice act, proposes to make it "unlawful for any osteopathic physician to use the word 'doctor' or any abbreviation thereof in any advertisement or sign after or before his name, or in connection with his practice without adding the words 'osteopathy,' 'osteopath' or 'osteopathic physician' thereto." H. 253 proposes, as a condition precedent to the issuance of a license to marry, that each party to a prospective marriage present a physician's certificate or a certificate from the Commissioner of Public Welfare that he or she is free from feeble-mindedness, insanity or venereal disease in a contagious stage. The bill proposes to limit a physician to $2 for executing such a certificate and making the necessary tests.

Illinois

Bills Introduced.—H. 224 proposes to appropriate $1,000,000 for the erection and operation of a state hospital for the care and treatment of poor persons affected with tuberculosis. H. 230 proposes to prohibit the employment or continuance in employment of a food handler unless he possesses a certificate from a licensed physician dated within the preceding ninety days certifying that he is free from communicable disease. H. 282 proposes to enact a separate chiropractic practice act and to create an examining committee to examine and license persons to practice chiropractic. The bill defines chiropractic as "the science of palpating and adjusting the articulations of the human spinal column by hand only." H. 293 proposes to enact a separate osteopathic practice act and to create an examining committee to examine and license persons to practice osteopathy. The bill defines osteopathy as "a system of practice of the healing arts in all its branches with therapeutics majoring in manipulation." Just what a license to practice osteopathy will permit the licentiate to practice is not clear but, as all applicants will be examined in surgery, obstetrics and gynecology, the license conceivably may permit the practice of obstetrics and the performance of all forms of surgery.

Indiana

Bill Passed.—H. 134 passed the house February 14, proposing, as a condition precedent to the issuance of a license to marry, that each party to a prospective marriage present a physician's certificate that he or she has been given such examination, including a standard serologic test, as may be necessary for the discovery of syphilis and that in the opinion of the physician the party is not infected with syphilis or, if so affected, is not in a communicable stage of that disease.

Bills Introduced.—H. 418 proposes that all actions against physicians, dentists or hospitals for malpractice, error, mistake or failure to cure, whether based on contract or tort, must be commenced within two years after the cause of action accrues. The bill proposes that a cause of action will be deemed to have accrued on the date of the act or neglect complained of. H. 477 proposes, among other things, to prohibit the retail sale or distribution of barbituric acid, aminopyrine, cinchophen, dinitrophenol or sulfanilamide except on the written prescription of a licensed physician, dentist or veterinarian. H. 494 proposes to require every physician, dentist and nurse on or before July 1, 1939, and at least once every twenty-four months thereafter, to submit a sample of his blood to an approved laboratory for a standard serologic test for syphilis. If the test indicates infection, the license of such person is to be suspended automatically and remain suspended so long as the disease is in a communicable stage.

Kansas

Bills Introduced.—H. 330 proposes to repeal existing laws regulating the possession and distribution of narcotic drugs and to enact what appears to be the uniform narcotic drug act. H. 375 proposes to impose a tax on the gross receipts derived from professional services, amounting to fifteen mills on the dollar.

Maine

Bills Introduced.—H. 1416 proposes to give to any hospital, not organized for profit and furnishing hospital service or materials to any patient injured by any accident not covered by the workmen's compensation act, a first lien on such proceeds of any accident and liability insurance policy issued by

any insurance company as may be due the patient, either directly or indirectly. H. 1432 and H. 1433 authorize the formation of nonprofit hospital service corporations to enter into contracts with subscribers for the rendering of hospital service to them through hospitals contracting to do so with the corporations in question. H. 1645 proposes to create a department of professional licensing to exercise all the powers and functions heretofore vested in the secretaries of the various licensing boards of the state, including the medical board, the osteopathic board, the chiropractic board and the dental board. H. 1706 proposes to require hospitals which are tax exempt or which receive any public funds to permit such osteopaths as are in good standing and are licensed to practice obstetrics and surgery to practice in their confines and to furnish laboratory service to outpatients of osteopaths. The present law requires such hospitals to admit osteopaths, subject to the approval of the hospital board, to treat their own paying patients and says nothing with respect to the laboratory service which must be furnished to outpatients of osteopaths.

Maryland

Bills Introduced.—H. 250 proposes to enact a law regulating the manufacture, distribution or advertising of foods, drugs, cosmetics and devices. H. 325 proposes to authorize the state board of health to establish such minimum standards and qualifications as it may deem necessary for laboratories in the state, except in Baltimore City, which make examinations in connection with the diagnosis and control of human diseases.

Minnesota

Bill Introduced.—S. 547 proposes to establish a state-wide system for the after-care of patients discharged from county and state tuberculosis sanatoriums.

Missouri

Bills Introduced.—S. 68 proposes, in effect, to permit hospitals to practice medicine through the agency of physicians in their employ. H. 264 proposes that a licensed physician or the owner or operator of a private sanatorium or hospital shall not be liable in damages for the restraint of any insane person or person of feeble or disordered mind by reason of having in good faith furnished care, treatment or attention to such person.

Montana

Bills Introduced.—H. 249 proposes to establish a state hospital to be known as the Montana State Infantile Paralysis Sanitarium. H. 265 proposes to authorize the state superintendent of public instruction to employ a specialist in the field of health and physical education to direct and supervise the organization of a state-wide program of health and physical education for public schools.

Nebraska

Bills Introduced.—Bill 392 proposes to condition the annual renewal of a license to practice osteopathy on the presentation of proof that the holder in the preceding year has attended at least two days of the annual "educational" program as conducted by the Nebraska State Osteopathic Association, or its equivalent. Bill 476 proposes a procedure whereby hospitals may be reimbursed by the state for treating indigent persons injured in motor vehicle accidents.

New Hampshire

Bill Introduced.—H. 327 proposes to create a commission on disability benefits to compile a report on the possibility of protecting individuals unemployed because of sickness or ill health.

New Jersey

Bill Enacted.—S. 61 has been enacted as Laws, 1939, chapter 13, appropriating $25,000 to the State Department of Health for the purchase and free distribution of antipneumococcus serum for the treatment of persons affected with pneumonia and financially unable to purchase the serum.

Bills Introduced.—A. 199 proposes to enact a separate chiropody practice act and to establish an independent board of chiropody examiners to examine and license persons to practice chiropody. The bill defines chiropody as "that branch of medicine and surgery which treats with ailments of the foot and leg and includes the diagnosis of the medical, surgical, mechanical, manipulative, and electrical treatments of all the ailments of the human foot and leg, excepting amputation of the leg, foot or toes, or the use of any anaesthetic other than local, or the treatment of congenital deformities by the use of the knife or radical operations for talipes valgus, or the treatment of varicose veins by injection or surgery." A. 200 proposes to authorize a judge of the court of common pleas, after notice and hearing, to commit a narcotic addict to any state, county or city institution for the care and treatment of his addiction.

New Mexico

Bills Passed.—S. 111 passed the senate February 20, proposing to permit the organization of corporations to operate hospital service plans and to provide that such a corporation may be organized by filing a certificate setting forth its name, its object, location and term of existence with the Superintendent of Insurance of the State, who is to endorse thereto his consent and file it in the Office of the State Corporation Commission. H. 259 passed the House February 22, proposing to make it a misdemeanor, punishable by a fine of from $100 to $500, for any person practicing the healing art to fail to specify on any sign or other advertising to the public the particular branch of the healing art which he practices. H. 51 passed the House January 27, proposing to require the governing authority of every public high school in the State to arrange for instruction in the public high schools concerning the prevention of venereal diseases.

New York

Bills Introduced.—S. 877 proposes to enact a self-styled New York uniform food, drug and cosmetic act to regulate the manufacture, sale or advertising of foods, drugs, cosmetics and devices. A. 1064 proposes to prohibit the practice of radiology except by licensed physicians, dentists, osteopaths and chiropodists, subject, however, to the conditions and limitations of their licenses. The bill proposes to define radiology as "diagnosis and/or treatment of diseases by means of exposure to roentgen rays and/or radium." A. 1090, to amend the law permitting a court whenever it is relevant to the prosecution or defense of an action to direct any party to the action and the child of any such party and the person involved in the controversy to submit to one or more blood grouping tests, proposes also to permit a court to order such a test "wherever it shall be relevant in any proceeding pending in a court of record." A. 1137 proposes to make it a misdemeanor for any hospital wholly or partly supported by public funds or exempt from taxation to refuse to permit any licensed physician the right to attend, treat and prescribe for any patient therein desiring his services.

North Carolina

Bill Passed.—S. 119, which passed the senate February 23, proposes to require the parent or parents or guardian of any child to have administered to the child between the ages of 6 months and 12 months an immunizing dose of a prophylactic diphtheria agent meeting the standard approved by the United States Public Health Service for such biologic products. This duty is also to be imposed on the parent or parents or guardian of any child between the ages of 12 months and 5 years who has not been previously immunized against diphtheria. If the parent or parents or guardian of such child are unable to pay for the services of a private physician for the immunization referred to, the appropriate county health officer is to administer the treatment.

North Dakota

Bills Introduced.—H. 267 proposes as a condition precedent to the issue of a license to marry that each party to the proposed marriage present a physician's certificate that he or she has been given such examination, including a standard serologic test, as may be necessary for the discovery of syphilis and that in the opinion of the physician the party either is not infected with syphilis or, if infected, is not in a stage of the disease which is or may become communicable to the marital partner. S. 194 proposes that an action may be commenced by the state, by any person who has a special interest in the action, against any person practicing, without a license, any profession requiring a license or certificate or other legal

authorization. One of the results of the enactment of this bill may well be to permit the issuance of injunctions to restrain the unlicensed practice of medicine. H. 281 proposes to authorize counties, either separately or in conjunction with one or more contiguous counties, to establish and maintain full time local health departments. H. 388 proposes to impose a tax of 2 per cent of the gross income received from any business, trade, profession or occupation.

Ohio

Bills Introduced.—S. 181 proposes to authorize the organization of corporations not for profit to establish and operate nonprofit hospital service plans whereby hospital service may be provided by hospitals with which such corporations have contracted to such of the public as become subscribers to said hospital service plans. H. 268, to revise and codify the laws relating to marriage, proposes, among other things, as a condition precedent to the issuance of a license to marry, that each party to a proposed marriage present a physician's certificate that he or she is free from venereal disease, epilepsy, feeblemindedness and insanity, as nearly as can be determined by thorough examination and by the application of the recognized clinical and laboratory tests of scientific research approved by the State Director of Health.

Oklahoma

Bill Passed.—S. 92 has passed the senate, proposing to require every physician attending a pregnant woman to take or cause to be taken a sample of her blood at the time of the first examination and to submit that sample to an approved laboratory for a standard serologic test for syphilis.

Bill Introduced.—H. 329 proposes to enact an independent naturopathic practice act and to create a board of naturopathic examiners to examine and license persons to practice naturopathy. The bill defines naturopathy as "The physiological and mechanical sciences, such as mechanotherapy, articular manipulation, corrective orthopedic gymnastics, neurotherapy, psychotherapy, hydrotherapy and mineral baths, electrotherapy, thermotherapy, phototherapy, chromotherapy, vibrotherapy, thalamotherapy and dietetics, which shall include the use of foods of such biochemical tissue-building products and cell salts as are found in the normal body; and the use of vegetable oils and dehydrated and pulverized fruits, flowers, seeds, barks, roots and vegetables uncompounded and in their natural state, and, added to the above definition, will include all methods now in use, as physiotherapy, Indian herb and simple remedy doctoring, physical culture, gyneacology [sic], autobiochemistry, colonictherapy and scientific massage and such methods as are taught in standard schools of Naturopathy."

Oregon

Bills Introduced.—S. 353 proposes that "Whenever any person shall receive hospitalization or medical or surgical care on account of any injury and such injured person shall claim damages from the party causing the injury, such hospital or person rendering medical or surgical care . . . shall have a lien upon any sum awarded the injured person in judgment or obtained by a settlement or compromise on the amount due for the reasonable value of such hospitalization or medical or surgical care rendered the injured person." This bill proposes to repeal the existing law which grants a similar lien to hospitals under the circumstances stated. H. 403, to amend the workmen's compensation act, proposes to make compensable an occupational disease arising out of and in the course of employment.

Bill Passed.—H. 415 passed the house February 20, proposing a procedure for the reimbursement of hospitals treating indigents injured in motor vehicle accidents.

South Dakota

Bills Introduced.—H. 247 proposes to require every physician attending a pregnant woman to take or cause to be taken a sample of her blood at the time of the first examination and to submit such sample for standard serologic tests for syphilis to the State Hygienic Laboratory of the State Board of Health or such other laboratories as are approved by the State Board of Health. H. 248 proposes to require as a condition precedent to the issuance of a license to marry that both parties to a proposed marriage present a certificate from a licensed physician that they are either free from syphilis or are not in a stage of the disease whereby it may become communicable, as nearly as can be determined by a thorough physical examination and such standard microscopic and serologic tests as are necessary for the discovery of syphilis.

Bill Enacted.—H. 10, the basic science bill, was approved by the governor February 23. The new law will require all applicants for licenses to practice any form of the healing art, as a condition precedent to examination and licensure by their respective professional boards, to pass examinations in anatomy, chemistry, physiology, pathology and bacteriology to be given by a board of basic science examiners.

Tennessee

Bills Introduced.—S. 547 and H. 739 propose to prohibit the retail sale and distribution of barbital except on the written prescription of a licensed physician, dentist or veterinarian. H. 758 proposes to grant to hospitals, treating persons injured through the negligence of others, liens on all claims, rights of action, judgments, compromises or settlements accruing to the injured persons because of their injuries.

Bills Passed.—H. 835, to supplement the medical practice act, has passed the house and senate, proposing to prescribe a procedure which must be followed in the revocation or suspension of licenses and to confer on the board of medical examiners stated powers with respect to such proceedings. The bill proposes that in such proceedings the accused physician must be given fifteen days' notice of the time set for the hearing and must be given an opportunity to prepare his defense, and is to be heard in person or by counsel, or both. The board is given the power in such proceedings to administer oaths, issue subpenas and to enforce the attendance and testimony of witnesses. A companion bill, S. 619, was introduced in the senate February 4. H. 609 passed the house February 22, proposing to require, as a condition precedent to the issuance of a license to marry, that each party to the proposed marriage present a physician's certificate that he or she has submitted to a physical examination, including a Wassermann and/or Kahn blood test, or other similar laboratory blood test, including a darkfield test where indicated, and that in the opinion of the physician the party is free from venereal disease.

Texas

Bill Introduced.—S. 81 proposes to appropriate $50,000 to the State Department of Health to assist in the eradication and control of pneumonia in the state.

Utah

Bills Introduced.—H. 225 proposes to authorize the organization of what the bill denominates "health cooperatives" to provide medical, dental, hospital and related services to their members. A cooperative may contract with or employ persons qualified to render any of the health services noted to its members. It may also contract for, own or operate such hospital, clinical, medical or dental facilities as it deems necessary. It is to be authorized to secure membership by advertisement, solicitation or any other means. H. 198 proposes to raise to $10 the annual license renewal fee required of physicians and surgeons, osteopaths, chiropractors and dentists.

Washington

Bills Passed.—S. 159 passed the senate February 21, proposing to make it unlawful for any hospital organized as a charitable institution to refuse to any licensed physician and surgeon the use of facilities therein or the right to attend patients therein, or refuse admittance to any patient for the direct or indirect reason that a particular physician and surgeon contracts to give medical service in consideration of payment of periodic premiums or dues or because of any physician's membership or nonmembership in any society or other lawful organization. H. 325 has passed the house and senate, proposing to amend the law approved by the governor February 3 prohibiting the retail sale or distribution of amytal, luminal, veronal, barbital, acid diethylbarbituric, or any of their salts, derivatives or compounds except on the prescription of a licensed physician, dentist or veterinarian. H. 325

proposes specifically that "It shall be unlawful for any person, firm or corporation to sell, give away, barter, exchange or distribute amytal, luminal, veronal, barbital, acid diethylbarbituric, or any of their salts, derivatives, or compounds of the foregoing substances, or any preparation or compound containing any of the foregoing substances, or their salts, derivatives or compounds, or any registered, trade-marked or copyrighted preparation or compound registered in the United States patent office . . . *containing more than one grain to the avoirdupois or fluid ounce of the above substances*" except under the written prescription of a licensed physician, dentist or veterinarian. Provisions of the law approved February 3 restricting the sale of para-amino-benzene sulfonamide, sulfanilamid, sulfamidyl, prontylin, prontosil, neo prontosil, edimalin, sulfonamid or any of their salts, derivatives or compounds are not changed by the provisions of H. 325.

Bills Introduced.—S. 263 proposes to enact a separate sanipractic practice act and to establish a sanipractic physicians' examining board, to examine and license persons to practice sanipractic. The bill proposes the following definition: "Sanipractic is the science and art of applied prophylactic and therapeutic sanitation, which enables the physician to direct, advise, prescribe or apply food, water, roots, herbs, light, heat, exercises active and passive, manipulation, adjusting tissue, vital organs and anatomical structure by manual, mechanical or electrical instruments or appliances; or other natural agency, to assist nature restore a psychological and physiological interfunction for the purpose of maintaining a normal state of health in mind and body. Above definition copyrighted 1919 for the purpose of protecting a separate and coordinate principle of healing." This bill was reported unfavorably to the senate February 22. S. 311 proposes to create a commission to investigate the organization, operation and control of hospital associations, medical service bureaus and other organizations supplying medical, hospital or surgical care. On the basis of its investigation and study the commission is to make recommendations to the 1941 session of the legislature respecting the regulation and control of persons or organizations engaging in the activities under study. S. 315 proposes to enact what it denominates the Washington uniform food, drug and cosmetic act to regulate the manufacture, distribution and advertising of foods, drugs, cosmetics and devices. H. 387 proposes to impose the following additional annual license fees on practitioners of the professions and occupations noted: drugless healing $3, medicine $5, midwifery $3 and veterinary medicine $3.

West Virginia

Bills Introduced.—S. 152 proposes that the provisions of the medical practice act "shall not be construed to apply to the practice of Christian Science, provided that the laws, rules, and regulations relating to communicable diseases and sanitary matters are not violated." H. 268, to amend the laws authorizing the sexual sterilization of certain socially inadequate inmates of state institutions, proposes to authorize the sexual sterilization of any inmate of a state institution afflicted with or suffering from any of the following conditions: (1) mental disease which may have been inherited and is likely to be transmitted to descendants; (2) feeblemindedness or mental deficiency, in any of its various grades; or (3) perversion or marked departure from normal mentality. The bill also proposes that any person found guilty of a carnal abuse of a female under 16 may, in addition to such other punishment or confinement as may be imposed by court, be subject to sexual sterilization. H. 352 proposes to make it unlawful for any person to use the prefix "Doctor" or "Dr." in connection with his name in any letter, business card, advertisement, sign or public display of any nature whatsoever, without affixing thereto suitable words or letters designating the degree which he holds.

Wisconsin

Bills Introduced.—S. 142 proposes to direct the board of control to establish a chiropractic ward at the Winnebago state hospital for the insane. A. 311, to amend the law requiring applicants for licenses to marry to present physicians' certificates as to freedom from syphilis, proposes (1) that such a certificate must be signed by a physician licensed to practice either in Wisconsin or in the state in which the applicant resides and (2) apparently, to limit to $3 the fee which a physician can charge for executing the certificate and making the necessary examination.

WOMAN'S AUXILIARY

Oregon

The auxiliary to the Oregon State Medical Society held a meeting of the board in Portland Nov. 2, 1938. Dr. Charles E. Sears gave an address on "State Medicine."

The auxiliary to the Josephine County Medical Society was organized Oct. 30, 1938, with eight charter members. Mrs. Byron G. Bailey, Grants Pass, was elected president.

The auxiliary to the Jackson County Medical Society met Oct. 19, 1938, having as guest the state president, Mrs. Otto C. Hagmeier, Seaside. The auxiliary will try to help furnish oxygen for patients who cannot afford it.

The November meeting of the auxiliary of the Klamath-Lake County Medical Society was spent making bibs and booties for the Doernbecher Memorial Hospital for Children, Portland.

The auxiliary of the Polk-Yamhill-Marion County Medical Society met November 8. Mr. R. Ivan Loveall, professor of history at Willamette University, Salem, spoke on "Conditions in Europe Today."

Texas

The auxiliary to the Travis County Medical Society met at the home of the president, Mrs. C. M. Darnall, Austin, October 18. Dr. B. J. Lloyd, director of the Austin and Travis County health unit, was speaker.

The auxiliary to the Wichita Medical Society held a breakfast meeting at the Woman's Forum Club House, Wichita Falls, October 11. Dr. C. W. Monroe of Electra spoke on socialized medicine.

Dr. S. E. Thompson of Kerrville spoke on socialized medicine at a meeting of the auxiliary to the Fifteenth District Medical Society and the society in Texarkana October 13.

Utah

The auxiliary to the Salt Lake County Medical Society met at the Lion House Social Center, Salt Lake City, October 17. Mrs. Henry Raile, president, presided. Members discussed "The Doctor of Yesteryear," "The Intern of Today," "The Dilemma," "We Might" and "Doctors' Day."

The auxiliary to the Carbon County Medical Society sponsored a public meeting held at the Elks Club, Price, recently. Dr. Edward L. Van Alstyn and Miss Jane West of the public health service discussed community health problems.——The officers of the state medical association and of the auxiliary held a joint meeting October 9 at Price with the Carbon County Medical Society and its auxiliary as hosts. Dr. L. A. Stevenson, Salt Lake City, discussed the program for medical legislation and Mr. W. H. Tibballs talked on socialized medicine.

The executive board of the auxiliary to the Utah Medical Association met at Salt Lake City October 13 with Mrs. Walter M. Stookey, president, presiding. The members voted to undertake the preparation of a history of the pioneer physicians of Utah.

Washington

The auxiliary to the Washington State Medical Association cooperated with the association in sponsoring "Your Health Exposition," held in Seattle in September. Exhibits from the American Medical Association and from local health organizations were shown. The exposition was attended by thousands of persons.

The auxiliary to the Cowlitz County Medical Society met at Longview in September. Dr. J. W. Henderson spoke on legislation and public health at a meeting November 16; the

program included a debate on "Resolved that socialized medicine would provide more adequate care for the public than our present system."

At a recent meeting of the auxiliary to the Pierce County Medical Society, Dr. Charles Engeles and Dr. W. G. Cameron spoke on legislative questions affecting the practice of medicine.

A meeting of the King County auxiliary was held November 21 in Seattle. "The Life of Chevalier Jackson" and "The Horse and Buggy Doctor" were reviewed. More than 100 members were present.

The auxiliary to the Walla Walla County Medical Society met October 14 at Walla Walla. Candidates for the state legislature presented their views on medical subjects. Mrs. R. E. Ahlquist, president of the auxiliary to the Washington State Medical Association, discussed plans for the year's work.

At a recent meeting of the auxiliary to the Yakima County Medical Society, Dr. Paul Lewis spoke on "The Six Most Common Diseases and Causes of Death." Mrs. J. C. Applewhite of Clarkston, parliamentarian for the State Federation of Women's Clubs, spoke on parliamentary procedure.

At a meeting of the auxiliary to the Spokane County Medical Society October 14, Dr. McIntyre, president of the society, talked on medical legislation. On November 11 "Socialized Medicine" was discussed.

MEDICAL ECONOMIC ABSTRACTS

CUT RATE EXAMINATIONS

A physician in Dayton, Ohio, has received the following letter from a "transport service bureau" in Detroit:

A trucking company has requested us to aid them in obtaining the services of a legally qualified physician in Dayton for the purpose of making medical examination of their drivers. They have about five employees to be examined. These examinations are made to ascertain the physical fitness of the drivers, who operate a motor vehicle on the public highway. They have eleven other terminals where examinations have been made or are in the process of being made by physicians, such as Toledo and Columbus, and the doctors in those cities do the work for $1 per examination, on the form attached hereto, which includes urinalysis but does not include blood test. Will you kindly advise if you will accept an appointment, and if so, we will then send you full instructions and supplies; also direct the employees to call at your office for these examinations. In event you accept the appointment, any other trucking company having employees to be examined in Dayton will be referred to you. Will you kindly give us an immediate reply as they are desirous of having these examinations made at once.

The copy of the Medical Examiner's Report which is attached to the letter calls for an examination of visual acuity, with and without glasses, for each eye, and an isolation and combination test for color blindness. The physician is also asked to state the degree of impairment of hearing on a percentage basis for each ear. In addition, he is asked to answer the question "Do you find evidence of *past* or *present* disease or impairment of the following" (italics in original):

(*a*) Eyes: 1. Right eye?
2. Left eye?
(*b*) Hearing: 1. Right ear?
2. Left ear?
(*c*) Nose or throat?
(*d*) Teeth and gums?
(*e*) Skin, thyroids, glands?
(*f*) Brain or nervous system?
(*g*) Lungs or pleurae?
(*h*) Pulse rate. 1. Before exercise?
2. After exercise?
(*i*) Heart: (Examine before and after 30 hops on one foot.)
1. Is there a murmur?
2. Is there dyspnea or other evidence of heart failure?
(*j*) Blood pressure. 1. Systolic?
2. Diastolic?
(*k*) Stomach or abdominal organs?
(*l*) Rupture?
(*m*) Piles?
(*n*) Maimed or deformed?
(*o*) Any restriction in motion of any joints?
(*p*) Syphilis?
(*q*) Venereal disease?
(*r*) Varicose veins or ulcers?
(*s*) Rheumatism?
(*t*) Any chronic or recurrent disease or deformity not included above?
Urinalysis: Reaction? Specific gravity? Albumin? Sugar?

The physicians are then instructed, with regard to any of these questions, "When answered 'Yes' give details."

It may be assumed that the "transport service bureau" expects accurate and complete information on all the items listed. If such an examination is actually made conscientiously by a physician who is willing to defend his results, it would require from one to more than two hours of time and possibly a consultation with or referral to some specialists for confirmation. The amount of laboratory work would, of course, vary with different persons, but a minimum must be performed, including a serum test for syphilis.

For all this the physician is to receive *one dollar*. By what intellectual legerdemain can it be concluded that the physician who undertakes such examinations will receive a fair fee for his services? And again, is it possible for any one to deliver a dependable service of the type requested for the price that is authorized?

MORBIDITY RISES UNDER BRITISH INSURANCE

"The National Health Insurance Act was designed principally as an instrument to improve the standard of curative medicine in general practice by replacing the old club system of contract practice," said Dr. A. B. Walker, regional medical officer, Department of Health for Scotland, in an address at the 1938 health congress at Portsmouth, published in the *Journal of the Royal Sanitary Institute* (**59**:511 [Jan.] 1939). "It was reasonable to hope that this act, together with the improved environmental services, by providing early and effective treatment would have some effect, not only in diminishing the amount and duration of disabling illness, but also an important preventive element. Yet, whilst sickness insurance on a national scale is a social service of proved value, it has not had these effects. Morbidity data available during the past few years show that incapacitating illness has tended to rise and with yearly fluctuations remains today at a new high level. This persistence of incapacitating illness amongst the insured population at a high general level, in spite of advances in preventive and curative medicine, is indicated in the successive Annual Reports on Incapacitating Sickness in the Insured Population, published by the Department of Health for Scotland. It is a fact which deserves the serious consideration of all interested in the public welfare."

UTAH STATE MEDICAL ASSOCIATION PREPAYMENT PLAN

The House of Delegates of the Utah State Medical Association has endorsed a plan of combined hospital insurance and cash indemnity for a limited amount of medical care. The hospital plan follows the general lines of existing plans except that anesthesia and laboratory and x-ray services are provided for on a cash indemnity basis instead of being included in hospital care. The annual premium for the hospital plan is $10 for an individual, $18 when one dependent is included, and $24 for an entire family regardless of size.

Only those who are covered by the hospital insurance plan are included in the cash indemnity plan for general medical care. The additional premiums are exactly the same as for hospital care, making $21.60 annually for an individual, $36 for an additional dependent, and $48 for a family for both hospital and medical care. The amounts to be reimbursed to the insured for various medical services are set forth in a schedule, and surgical services are limited to one major and one minor operation per member in a single year.

Enrolment is confined to employed persons and to groups which may be either employees of a common employer or "members of church and fraternal groups and their dependents agreeing to collect the necessary membership fees by assessment for subscription, remitting through a designated agent."

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Society News.—A joint meeting of the southwestern and northwestern divisions of the state medical association was recently addressed in Tuscaloosa, among others, by Drs. Gerald H. Teasley, Athens, on "Nitrous Oxide-Oxygen in Rural Obstetrics"; Kellie N. Joseph, Birmingham, "Diagnosis and Treatment of Pleural Effusions"; William M. Bland, Tuscaloosa, "Preoperative Diagnosis of Gallbladder Disease Made Possible Through Laboratory Analysis in Conjunction with Fluoroscopic Examination of the Gallbladder and Duodenum"; Benjamin T. Beasley, Atlanta, Ga., "Surgical Management of Damaged Genital Supports in the Female," and William G. Harrison Jr., Birmingham, "Therapy of Heart Disease." The luncheon meeting was addressed by Richard C. Foster, D.C.L., president of the University of Alabama, and Drs. Stuart Graves, University, William D. Partlow, Tuscaloosa, and Seale Harris, Birmingham.

ARKANSAS

District Meeting.—The Fifth Councilor District Medical Society met at El Dorado January 11. The speakers included Drs. Richard B. DeLee and Harold G. F. Edwards, both of Shreveport, La., on "Bronchial Asthma" and "Carcinoma" respectively.

Project Approved for Training Center.—The field experience center operated by the state board of health at Morrilton has been approved as a health training center by Vanderbilt University, Peabody College and the Medical College of Virginia, newspapers recently reported. The center is intended to give actual training to persons engaged in public health work in the state.

CALIFORNIA

Changes in Health Officers.—Dr. Dwight M. Bissell, Pittsburg, has been appointed health officer in Monterey County, succeeding Dr. Roy M. Fortier, Salinas, who has taken a leave of absence for one year on account of illness. Dr. Bryson E. Cox has been named city health officer of Coalinga.

Diphtheria Increases in Adults.—In 1938 forty-three cases of diphtheria were reported in San Francisco with nine deaths; fourteen cases and four deaths were in adults. A statement from the city health department offers for comparison the 360 cases of diphtheria reported in 1929, including forty-three cases in adults; of the seventeen deaths, only two occurred in the adult group. The program for immunization for diphtheria control among the age group from 6 months to 15 years has been nearly accomplished in the last fifteen years, but the state department says that this has meant a higher incidence of diphtheria in nonimmunized adults than among children in the population of San Francisco today.

Tuberculosis Hospitals for Indians.—A new fifty bed annex for the treatment of tuberculous Indians was dedicated August 6 at the Weimar Joint Sanatorium, Weimar, and one of thirty-six beds at the Wish-i-ah Sanatorium near Auberry, Fresno County, Aug. 13, 1938. Constructed on land deeded to the federal government, each unit cost $70,000, it was reported. Both are PWA projects sponsored by the Office of Indian Affairs, U. S. Department of Interior. The Weimar annex will be operated by the hospital central committee of the Weimar Joint Sanatorium under the professional and administrative direction of Dr. Mildred E. Thoren, superintendent and medical director, while the unit at Wish-i-ah will be operated by the county of Fresno under the supervision of Dr. Everett Morris, superintendent and medical director. At Weimar Indians residing in the fourteen counties comprising the sanatorium group will be given preference in admission while Indians of Fresno County will be given preference at Wish-i-ah. Indians who are recognized wards of the government may be admitted if space is available. In both cases the federal government will reimburse the counties at the per diem cost determined as a routine by the institutions. Applications for admission will be passed on by the superintendent of the Sacramento Indian Agency, Sacramento; technical assistance will be given by the district medical director of the U. S. Indian Service in San Francisco. Prior to the completion of these units a hospital at Fort Bidwell, Modoc County, was the only institution of the U. S. Indian Service in the state available for the care of tuberculous Indians. It has a total of thirty-eight beds, thirty of which are available for the treatment of tuberculosis. There is now a maximum of 120 beds available for these Indians in federal institutions in the state, serving an estimated Indian population of 28,000. During the calendar year 1937 there were sixty-seven deaths from tuberculosis among the Indian population of the state; based on this number of deaths there are now about two beds for each annual death from the disease.

COLORADO

Sewall Foundation Lectures.—Dr. Russell M. Wilder, Rochester, Minn., lectured at the University of Colorado School of Medicine, Denver, under the auspices of the Henry Sewall Foundation, February 7-8. His subjects were "Arteriosclerosis and Diabetes" and "Diabetes and Endocrine Glands Other Than the Pancreas."

CONNECTICUT

Society News.—Dr. Herbert C. Miller Jr., New Haven, among others, presented "A Study of Infant Mortality in Cesarean Section" before the Yale Medical Society, New Haven, February 8. Dr. Norman E. Freeman, Philadelphia, discussed "Circulation in Surgical Shock" before the society January 8.

Report of Summer Round-Up.—According to the state department of health, 3,476 children were examined in 226 round-ups held during the summer of 1938. The group was 71 per cent of all children entering the 314 schools in the towns participating in the round-ups. Among the total examined, 2,594 children were found to have 5,214 physical defects, of which 1,517 were serious enough to be referred to family physicians. Seventy-eight per cent, or 2,737 of the children examined, suffered from dental defects. During the fall, reports of corrections of defects have been returned and tabulated. These reports, although incomplete, show that to date 850, or 16 per cent, of the physical defects found have been corrected or improved, while 354, or 13 per cent, of the children received dental care.

DELAWARE

Society News.—Dr. Robert P. Bay, Baltimore, addressed the New Castle County Medical Society in Wilmington recently; the title of his paper was "The Surgical Abdomen." Dr. Joseph C. Birdsall, Philadelphia, recently discussed "Renal Pathology in Urinary Tract Obstruction" before the society. Dr. Amos R. Koontz, Baltimore, addressed the society January 17 on "The Use of Fascia in Surgery."

GEORGIA

Society News.—Dr. Avary M. Dimmock gave a clinical talk on "Sulfonamide and Specific Serum in Pneumonia" before the Fulton County Medical Society in Atlanta January 19, and Dr. Grady E. Clay read a paper entitled "Eyeground Changes in Hypertension and Encephalitis," both of Atlanta. Dr. Albert A. Rayle read a paper entitled "Radiology and the Right Lower Quadrant" before the society, Atlanta, February 2.

Dr. L. C. Fischer's Gift to Atlanta.—Property valued at nearly a million dollars was recently given to the city of Atlanta by Dr. Luther C. Fischer, including the Crawford W. Long Memorial Hospital, established in 1908 by Dr. Fischer and the late Dr. Edward C. Davis. Dr. Fischer gave also his 138 acre estate in Chamblee to the same board of trustees who will handle the hospital for the public. Ten acres of the estate is planted in roses; the gardens are endowed with $200,000 for maintenance. Dr. Fischer stipulated that the hospital must be operated for the benefit of families of modest means, persons who are unable to pay the standard costs of hospitalization and unwilling to accept charity but who will pay only what they are able.

ILLINOIS

Society News.—Dr. Raymond A. Tearnan, Decatur, discussed "Ovarian Dysfunction and Treatment" before the Franklin County Medical Society in Benton January 26.——At a meeting of the Douglas County Medical Society in Villa Grove January 27, Dr. Thomas B. Williamson, Mount Vernon, spoke on "The Significance of Prenatal Care."——A symposium on fractures of the neck of the femur was presented before the

Sangamon County Medical Society January 5 by Drs. Frank A. Norris, Ivan E. Brouse and Carl Black, all of Jacksonville. ——Dr. James Duffy Hancock, Louisville, Ky., discussed "Abdominal Tumors in Children, Surgical Treatment" before the St. Clair County Medical Society in East St. Louis January 5.——A symposium on physiologic action of insulin and metrazol as used in shock therapy was presented before the Illinois Psychiatric Society, Chicago, January 5 by Drs. Samuel Soskin, Ernst Gellhorn and Ralph W. Gerard. Dr. H. Douglas Singer delivered his presidential address on "Relationship Between Personality and Psychosis."——At a meeting of the Madison County Medical Society in Edwardsville February 3, Dr. Charles J. Drueck, Chicago, among others, spoke on "Pruritus Ani."

Chicago

Studies in Malaria.—The Rockefeller Foundation has made a grant of $2,000 to continue for the year 1939 the studies in malaria conducted by William H. Taliaferro, Ph.D., chairman of the department of bacteriology and parasitology, and dean of the Division of Biological Sciences, University of Chicago. The foundation has supported the work of Dr. Taliaferro and his associates for a number of years. The studies are concerned with analysis of the mechanisms by which the body resists malarial infection and with the physiologic and genetic studies of the mosquitoes which transmit malaria and of malarial parasites.

Society News.—Dr. Irvin Abell, Louisville, Ky., President, American Medical Association, lectured at the Chicago Woman's Club February 22 under the auspices of the public health committee of the Chicago Woman's Club, the Chicago Medical Society and the Chicago chapter of the American College of Surgeons; his subject was "The Position of Medicine in Our Present Day Culture."——Dr. William D. Stroud, Philadelphia, discussed "Coronary Disease Including Angina Pectoris" at the annual meeting of the Chicago Heart Association January 31.——Dr. Lewis Gregory Cole, New York, discussed "Dyspnea of Silicosis: What Causes It?" before the Chicago Roentgen Society February 16. —— Among others, Ludwig R. Kuhn, Ph.D., presented "Some Observations on Experimental Cryptococcus Infection" before the Chicago Pathological Society February 13.——The speakers before the Chicago Neurological Society February 16 included Dr. Mark A. Foster, Madison, Wis., on "Acute Encephalomyelitis, Equine or Avian?" and Drs. Harry A. Paskind and Meyer Brown, "Constitutional Differences Between Deteriorated and Nondeteriorated Patients with Epilepsy: IV. Dactylographic Studies."—— The Chicago Ophthalmological Society was addressed February 20 by Drs. Sanford R. Gifford and Gilbert H. Marquardt, among others, on "Central Angiospastic Retinopathy."——Dr. Louis E. Prickman, Rochester, Minn., discussed "Asthma and the Stenosed Bronchus Syndrome" before the Chicago Society of Allergy February 20.——Dr. Ralph Hess Kunstadter presented the inaugural thesis before the Chicago Pediatric Society February 21 on "The Waterhouse-Friderichsen Syndrome."

INDIANA

Members of State Board Reelected.—The following officers of the Indiana State Board of Medical Registration and Examination were reelected at the annual meeting January 10 in Indianapolis: Drs. Jacob T. Oliphant, Farmersburg, president; Norris E. Harold, Indianapolis, vice president; Jesse W. Bowers, Fort Wayne, secretary, and William C. Moore, Muncie, treasurer.

Personal.—Dr. Ernst L. Schaible, Gary, has been elected mayor of Gary.—— Dr. Otho R. Lynch, Peru, has been appointed medical director of the Wabash Valley Sanatorium; he was formerly superintendent of the Longcliff State Insane Hospital near Logansport.——James F. Glore, medical artist at the Indiana University Medical Center, was recently presented with the Indianapolis Junior Chamber of Commerce distinguished service award for "outstanding community service during 1938."

Society News.—At a meeting of the Tippecanoe County Medical Society in Lafayette January 10 Dr. Henry O. Mertz, Indianapolis, spoke on "Traumatic Injuries to the Urinary Tract."——The Gibson County Medical Society was addressed in Princeton January 9 by Dr. Robert R. Acre, Evansville, on "The Prostate After Age 40."——Dr. Charles J. Cooney, Fort Wayne, discussed hematuria before the Fort Wayne Medical Society January 3.—— The Indianapolis Medical Society was addressed by Drs. Murray N. Hadley and Rollin H. Moser, both of Indianapolis, February 28 on "The Surgical Treatment of Intractable Peptic Ulcer" and "Medical Aspects of Peptic and Duodenal Ulcer."

IOWA

Annual Tuberculosis Meeting. — The Iowa Tuberculosis Association will hold its annual meeting at the Fort Des Moines Hotel, Des Moines, March 10, with the following speakers included on the tentative program:

Dr. Nevin Boyd Anderson, Des Moines, Surgical Treatment of Tuberculosis.
Dr. John Russell, Des Moines, Pneumoperitoneum.
Dr. Charles K. McCarthy, Des Moines, The Cooperative Case-Finding Program.
Dr. James A. Downing, Des Moines, Use of the Bronchoscope in Diseases of the Chest.
Dr. Ira D. Nelson, Toledo, Films of Indian Children.
Dr. John C. Parsons, Des Moines, Blood Findings in Tuberculosis.
Dr. Irving H. Borts, Iowa City, Sputum Determinations in Tuberculosis.
Dr. Lee F. Hill, Des Moines, Significance of the Primary Infection.

Dr. Horton R. Casparis, Nashville, Tenn., will address the noon luncheon.

LOUISIANA

Personal.—Dr. Emmanuel F. Salerno was recently elected chief medical officer of the Orleans Parish school board, filling the vacancy caused by the death of Dr. John Signorelli.—— Dr. Charles A. Bahn, New Orleans, was awarded the annual cup by the Rotary Club for "outstanding civic services," which were his part in reorganizing the Louisiana Society for the Prevention of Blindness.

Changes in Health Officers.—Dr. Murphy M. Sims has been appointed director of the Vermilion Parish health unit, Abbeville, succeeding Dr. Benjamin O. Morrison, who was assigned as director of the Acadia Parish unit, Crowley.—— Dr. Herbert E. Cannon, Covington, has been chosen to head a new health unit to be started in St. Tammany Parish, newspapers recently reported; he will take a special course of training before taking over his new position.

MAINE

Society News.—Piscataquis County Medical Society was the first society, for the second successive year, to send to the Maine Medical Association 100 per cent payment of dues.—— Dr. Samuel A. Levine, Boston, will discuss "The Auscultation of the Heart" before the Kennebec County Medical Association in Gardiner April 20.

MICHIGAN

New Hospital Service Plan.—The Michigan Society for Group Hospitalization was incorporated Dec. 8, 1938, and was expected to begin functioning February 15, according to *Detroit Medical News*. The new society was organized by the Michigan State Hospital Association with the approval of the Michigan State Medical Society. Provisions have been made for a board of trustees not to exceed twenty-five members, officers to be Mr. William J. Griffin, a trustee of the Highland Park General Hospital, president; Mr. John R. Mannix, formerly assistant director of the University Hospitals of Cleveland, director; Dr. Joseph Thomas Stewart Hamilton, Detroit, vice president, and Dr. Warren L. Babcock, Detroit, treasurer. According to the *Detroit Medical News*, the society will provide hospital service for twenty-one days in any one year in a ward room at the following rates:

Individual, 60 cents a month; husband and wife, $1.20 a month; entire family (with all children from age 1 year to 19 years) $1.50 a month. Service in semiprivate room will be available at the following rates: individual, 75 cents a month; husband and wife, $1.50 a month; family, $1.50 a month.

Hospital service will include room and board, general nursing, operating room service, including anesthesia when administered by a salaried employee of the hospital, routine clinical laboratory service and ordinary drugs and dressings. It will not include the services of the subscriber's attending physician or surgeon nor special nurses or their board. The plan provides for free choice of physician, and all admissions to the hospitals will have as a prerequisite the certification by a physician that the hospital service is needed.

MINNESOTA

Hospital News.—Dr. Ian Snapper, professor of medicine, University of Amsterdam, gave a Mayo Foundation lecture in Rochester January 16 on "Clinical Investigations on the Influence of Organic Iodine Compounds on the Activity of the Thyroid Gland." Dr. Maurice B. Visscher, Minneapolis, delivered a foundation lecture January 19 on "Recent Studies on Energetics of the Failing Heart."

Society News.—Dr. Charles B. Wright addressed the Hennepin County Medical Society in Minneapolis February 8 on "The American Medical Association: Its History and Background." Dr. Wyman C. C. Cole, Detroit, spoke February 6 on "Etiologic Factors in Neonatal Asphyxia."——Dr. John Albert Key, St. Louis, addressed the annual foundation dinner and meeting of the Minneapolis Surgical Society February 2 on "Treatment of Compound Fractures."

Osteopath Fined for Practicing Medicine.—John L. Moore, a licensed osteopath with offices at Windom, pleaded guilty Dec. 22, 1938, to practicing medicine without a license and was sentenced to pay a fine of $250 and court costs of $7, which he paid. The investigation disclosed that Moore was prescribing and furnishing medicine to patients for internal use. The board also showed that as far back as 1930 Moore had been warned to confine his practice to osteopathy.

MISSISSIPPI

Changes in Health Officers.—Dr. Norris C. Knight has resigned as director of the Coahoma County health unit, after five years in the position, to take charge of the unit in Lauderdale County, with headquarters in Meridian. Dr. Guy R. Post, Holly Springs, health officer of Marshall County, will succeed Dr. Knight in Coahoma County.

Society News.—Dr. Conley H. Sanford, Memphis, Tenn., among others, addressed the seventy-third annual meeting of the Clarksdale and Six Counties Medical Association in Clarksdale recently on "Clinical Manifestations of Vitamins."——The Northeast Mississippi Thirteen-County Medical Society was addressed at its fourth quarterly meeting in Tupelo recently by Drs. Rome T. Dabbs, Verona; Frank M. Davis, Corinth; Van Buren Philpot, Houston, "Some Experiences in Simple Methods of Treating Fractures"; Conley H. Sanford, Memphis, "Types and Treatment of High Blood Pressure," and Henry King Wade, Hot Springs, Ark., "Urinary Infections with Special Reference to Their Medical Management."

MISSOURI

Annual Medico-Military Symposium.—The Kansas City Southwest Clinical Society will hold its annual spring medico-military symposium in the auditorium of the Jackson County Medical Society, Kansas City, March 13-14. The speakers will include:

Dr. Frank D. Dickson, Low Back Pain from the Orthopedic Standpoint.
Dr. Ira H. Lockwood, Some Obscure Causes of Low Back Pain.
Dr. Fernando I. Wilson, Nonsurgical Treatment of Hemorrhoids.
Dr. Peter T. Bohan, Nerve Root Disturbances Simulating Organic Diseases of Viscera.
Dr. Cyrus C. Sturgis, Ann Arbor, Mich., The Historical Development of Our Knowledge and the Present Status of Blood Transfusion.
Dr. Paul M. Krall, Kansas City, Kan., The Role of Certain Biological Compounds Normally Present in the Body in the Possible Etiology of Carcinoma.
Dr. Donald R. Black, Pathology and Physiology as Applied to the Treatment of Diabetes.
Dr. Arthur Lloyd Stockwell, Management of Urinary Tract Infections.
Dr. Joseph E. Welker, Diagnosis and Treatment of Cardiac Neuroses.
Dr. Albert N. Lemoine, Treatment of Traumatic Injuries to the Eyeball.
Dr. Harry C. Lapp, Common Complications in Gallbladder Disease.
Dr. Arthur C. Essen, Avitaminosis—A Study of Correlation.
Dr. Hubert M. Parker, Indications and Contraindications for Calcium Therapy.
Dr. John H. Ogilvie, Recognition of the Acute Abdomen Due to Trauma.
Dr. John L. Myers, The Various Methods of Examining the Larynx (color movie).
Dr. John P. Beeson, Omaha, Picture-Map Reading (sound movie).
Dr. Lindsay S. Milne, The Role Played by Arthritis in the Aggravation of Injuries.
Dr. Ralph R. Coffey, Evaluation of the Signs and Symptoms in the Differential Diagnosis of the Acute Abdomen.
Dr. La Verne B. Spake, Kansas City, Kan., Complications and Sequelae of Sinusitis.
Dr. Thomas G. Orr, Acute Nonmalignant Intestinal Obstruction.
Dr. Sumner L. Koch, Chicago, Infections of the Hand.
Dr. Frederick B. Campbell, Significance of Bleeding from the Rectum and Treatment of the Simple Types.
Dr. Caryl R. Ferris, Fundamentals in the Treatment of Pneumonia.
Dr. James R. Elliott, Treatment of Simple Fractures of the Wrist and Ankle.
Dr. Paul F. Stookey, Staphylococcus Septicemia—The Use of Staphylococcus Antitoxins in Its Treatment.
Dr. Edward T. Gibson, Emotional Factors in Visceral Symptomatology.
Dr. Frank R. Teachenor, Spinal Cord Injuries.
Dr. Ferdinand C. Helwig, Trauma and Malignancy.

A joint meeting will be held with the Jackson County and Wyandotte County medical societies Monday evening with Dr. Charles R. Reynolds, surgeon general, U. S. Army, Washington, D. C., and Dr. Sturgis as the speakers. Their subjects will be "The Present Responsibilities of the Medical Department of the Army" and "Some Common Sense Remarks Concerning the Menace and Treatment of Obesity" respectively. Tuesday evening a dinner with the Kansas City Academy of Medicine will be addressed by Dr. Harry P. Smith, professor of pathology, State University of Iowa College of Medicine, Iowa City, on "Recent Progress in the Study of Hemorrhage."

NEW JERSEY

Society News.—Dr. Harvey F. Doe, Montclair, of the state department of health, addressed the Cape May County Medical Society, Cape May Court House, January 13, on pneumonia.——Dr. Elmer P. Weigel, Plainfield, addressed the Morris County Medical Society, Greystone Park, January 19, on osteogenic sarcoma.——Drs. Bret Ratner and Marion B. Sulzberger, New York, addressed the Passaic County Medical Society, Paterson, January 12 on "Abdominal and Digestive Manifestations of Allergy in Children" and "Allergic Skin Disease of Children" respectively.——Dr. Edward H. Dennen, New York, addressed the Union County Medical Society, Elizabeth, January 11, on "Choice of Instruments in Delivering with Forceps."——Dr. Irvin E. Deibert, Camden, was elected president of the Society of Surgeons of New Jersey at the annual meeting in Newark January 28 and Dr. Walter B. Mount, Montclair, was reelected secretary. Clinics were held at St. Michael's Hospital and the Newark Eye and Ear Infirmary in the morning and after luncheon at the Robert Treat Hotel motion pictures of operations were shown.

NEW YORK

Society News.—Dr. Mark Williams, Binghamton, addressed the Broome County Medical Society, Binghamton, February 14 on "Postpneumonic Empyema in Children." Dr. Alexander D. Langmuir, Albany, assistant director of the bureau of pneumonia control, New York State Department of Health, addressed the society January 10 on "Higher Types of Pneumonia."——Dr. Russell L. Cecil, New York, addressed the Medical Society of the County of Albany, February 15 on "Modern Aspects of Pneumonia Therapy."——Dr. Samuel A. Levine, Boston, addressed the Medical Society of the County of Westchester, White Plains, February 21 on auscultation of the heart.

New York City

Exhibit on Hormones.—A preview of a sex hormone demonstration to be exhibited in the Hall of Science at the Golden Gate Exposition in San Francisco was held at the Hotel Astor January 23 by the Schering Corporation, which was invited to prepare the exhibit. The central feature is a transparent female figure showing the manner in which endocrine secretions affect the various organs of the body.

New Type of High Voltage X-Ray Tube Developed.—A million volt x-ray tube small enough so that it does not require a special building has been developed for the new building of Memorial Hospital by the General Electric Company, according to a recent announcement. The new mechanism can be installed with much less expense and it is much less heavy than previous tubes of this voltage. The tube itself is 56 inches long and 3½ inches in diameter and is mounted vertically in the space usually occupied in x-ray machines by the iron core. Tube and transformer are enclosed in a cylindric tank of two sections of steel bolted together. A new feature is the use of gas instead of oil as the insulating fluid; it was said that about 100 pounds of gas replaces about 12,000 pounds of oil. There are no moving parts and the control is entirely electrical.

Personal.—Dr. Royal Whitman, London, England, formerly of New York, was recently made an honorary fellow of the Royal College of Surgeons of England.——Dr. Edward A. Flemming, Forest Hills, was honored at a dinner Dec. 15, 1938, in tribute to his work during ten years as trustee of the Medical Society of the County of Queens.——Dr. Philip E. Smith Jr., Brooklyn, was honored at a dinner January 18 in recognition of his thirty years of practice in the Saratoga and Bushwick sections. Members of the surgical staffs of the Bushwick and Evangelical and Deaconess hospitals and other friends arranged the dinner.——Dr. Laura M. Long Riegelman, for the past nineteen years chief of the bureau of child hygiene in Brooklyn, retired December 31 after forty years of service with the city department of health. She was honored at a dinner given by her colleagues.

Society News.—Drs. Alfred F. Hocker and John V. Blady addressed the New York Roentgen Society January 16 on "Sialography—Its Technic and Application in the Diagnosis of Diseases of the Salivary Glands."——Drs. Baldwin H. E. W. Lucke, Philadelphia, and Thomas Francis Jr. addressed the New York Pathological Society January 26 on "Reaction of

the Nasal Mucosa to Infection with the Virus of Epidemic Influenza" and "Carcinoma in Frogs: Its Etiologic Relation to a Virus and Its Habits of Growth in Vivo and in Vitro" respectively.——Friedrich Gudernatsch, Ph.D., addressed the Bronx Pathological Society January 17 on "Genetic and Hormonal Factors in Development and Differentiation of Sex."——Dr. Elaine P. Ralli addressed the Bronx County Medical Society January 18 on "The Role of Nutrition in Health and Disease."——Drs. Samuel S. Rosenfeld and Leo Wilson, among others, addressed the Bronx Gynecological and Obstetrical Society January 23 on "Presacral Sympathectomy for Intractable Pelvic Pain" and "Uterine Contractibility" respectively.

NORTH CAROLINA

Society News.—Dr. Emil Novak, Baltimore, addressed the Buncombe County Medical Society, Asheville, January 16, on "Gynecological Endocrinology."——Dr. Lester A. Crowell Jr., Lincolnton, among others, addressed the Catawba Valley Medical Society in Morganton, January 10 on "The Practical Handling of Adult Uncomplicated Diabetes Mellitus."

Changes in Health Officers.—Dr. Joseph A. Morris, Oxford, has resigned as health officer of Granville County on account of ill health. In point of service he was said to be the oldest health officer in the state. He has served in Granville County since 1919.——Dr. Henry A. Brandon, Yadkinville, has been chosen health officer of Yadkin County, succeeding Dr. Locksley S. Hall.——Dr. Ralph J. Sykes, Mount Airy, health officer of Surry County, has been appointed health officer of Halifax County. He succeeds Dr. Robert S. McGeachey, Weldon, who has gone to Craven County. In Surry County Dr. Robert B. C. Franklin, Chapel Hill, will succeed Dr. Sykes.

OHIO

New State Health Officer.—Dr. Roll H. Markwith, Akron, health officer of Summit County, has been appointed state health officer, succeeding Dr. Walter H. Hartung. Dr. Markwith graduated from Ohio State University College of Medicine, Columbus, in 1917 and has been head of the Summit County health unit since 1921.

In Memory of Dr. Todd.—Western Reserve University School of Medicine, Cleveland, sponsored a memorial meeting January 15 for the late Dr. T. Wingate Todd, Henry Willson Payne professor of anatomy, who died Dec. 28, 1938. Dr. Elliott C. Cutler, Boston, former professor of surgery at Western Reserve, gave an appreciation of Dr. Todd. Dr. Roy W. Scott spoke for the medical school; Elbert J. Benton, Ph.D., for the graduate school; William C. Stillson, D.D.S., for the school of dentistry; the Rev. Joel B. Hayden for the Brush Foundation; Dr. Clyde L. Cummer for the Academy of Medicine of Cleveland and Howard Whipple Green for the Cleveland Health Council. Dr. Jerome Gross arranged a musical program. Winfred G. Leutner, LL.D., president of the university, presided.

Society News.—Dr. Miles Tischer Hoerner, Dayton, discussed "Diagnosis and Treatment of Jaundice" before the Greene County Medical Society, Xenia, January 5.——Dr. Frank C. Andrus, Springfield, addressed the Clark County Medical Society, Springfield, February 16 on "Significance of Clinical Findings in Nephritis."——Dr. Curtis F. Garvin, Cleveland, addressed the Lorain County Medical Society, Lorain, January 10 on "Complications of Sulfanilamide Therapy."——At a meeting of the Tuscarawas County Medical Society January 12 in New Philadelphia Drs. George L. F. Sackett and Harry L. Farmer, Cleveland, spoke on "Spontaneous Pneumothorax" and "Urography" respectively.——Dr. Clayton G. Weigand, Indianapolis, addressed the Columbus Academy of Medicine February 6 on "Practical Applications of Vitamin Therapy."

OKLAHOMA

Personal—Dr. William H. Kaeiser, McAlester, has been appointed health superintendent of Pittsburg County.——Dr. Calvin E. Bradley, Tulsa, has been appointed to the state board of medical examiners.

Society News.—Dr. E. Rankin Denny, Tulsa, addressed the Garfield County Medical Society, Enid, January 26, on allergy.——Dr. Felix M. Adams, Vinita, addressed the Tulsa County Medical Society, Tulsa, February 27, on "Insulin Treatment of Dementia Praecox."

New State Health Commissioner.—Dr. Grady F. Mathews, recently in charge of a health district with headquarters at Tahlequah, has been appointed state health commissioner, replacing Dr. Charles M. Pearce. Dr. Mathews, who was selected from a group of four physicians suggested by the Oklahoma State Medical Association, graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1925.

OREGON

Graduate Course in Ophthalmology and Otolaryngology.—The Oregon Academy of Ophthalmology and Otolaryngology and the University of Oregon Medical School will present their fourth annual spring postgraduate course in ophthalmology and otolaryngology in Portland April 3-8. The guest lecturers will be Drs. John J. Shea, Memphis, Tenn., and Webb W. Weeks, New York. Additional information may be obtained from Dr. Paul Bailey, 929 Medical Dental Building, Portland.

PENNSYLVANIA

Society News.—Dr. Harold L. Foss, Danville, addressed the Delaware County Medical Society, Chester, February 9, on "Status of Cancer of the Colon in Pennsylvania."——A program on pneumonia was presented before the Fayette County Medical Society February 2 by Drs. James A. Mansmann, Philip G. Leavy and Murray B. Ferderber, all of Pittsburgh.——Dr. William W. Bolton, Upper Darby, chief of the division of syphilis and genitoinfectious diseases, Pennsylvania State Department of Health, addressed the McKeesport Academy of Medicine, January 23, on syphilis.——At a meeting of the Lycoming County Medical Society, Williamsport, February 10, the speakers were Drs. James Stanley Smith, on "Use and Abuse of Sulfanilamide, with Reference to Its Use in Treatment of Gonorrhea"; William D. Angle, "Use of the Ophthalmoscope by the General Practitioner" and Louis E. Audet, "Obesity"; all are from Williamsport.——Dr. Carl E. Ervin, Harrisburg, addressed the Lebanon County Medical Society February 14 on undulant fever.

Philadelphia

Epidemic of Respiratory Disease.—Schools and hospitals reported a wave of respiratory infections during February. Calls for nurses increased from 40 to 50 per cent, it was reported from private exchanges and the visiting nurses' service. Hospitals reported full occupancy and many illnesses among their staffs, according to newspaper accounts.

Personal.—Dr. Paul B. Cassidy has been appointed director of St. Vincent's Hospital for Women and Children, succeeding Dr. John A. McGlinn, who becomes director emeritus.——Dr. Ludwig Loeb, for many years medical director of the National Stomach Hospital, was honored at a dinner given by the medical staff and board of directors of the hospital January 26. Mr. Arleigh P. Hess, president of the hospital board, presented to Dr. Loeb a silver plaque. Dr. Loeb is reported to be the only surviving founder of the hospital.

Fourth Postgraduate Institute.—The Philadelphia County Medical Society will present its fourth annual Postgraduate Institute March 13-17 at the Bellevue-Stratford Hotel. The subject this year is "Blood Dyscrasias and Metabolic Disorders." About ninety Philadelphia physicians will take part in the program, presenting papers from fifteen to twenty minutes long morning and afternoon. On the first day there will be a luncheon at which Dr. Francis F. Borzell, president of the county medical society, will preside and the speakers will be the Hon. S. Davis Wilson, mayor of the city; Dr. Charles H. Henninger, Pittsburgh, president-elect of the Medical Society of the State of Pennsylvania, and Dr. Rufus S. Reeves, director of the institute. At a dinner of the county society March 15 Dr. James S. McLester, Birmingham, Ala., will deliver the J. Chalmers Da Costa Oration on "Borderline Nutritional States."

Pittsburgh

Chamber of Commerce Endorses Organized Medicine.—The Pittsburgh Chamber of Commerce recently passed a vote of confidence in organized medicine. Copies of the action were sent to the President, Senators and Congressmen.

Society News.—Speakers before the Allegheny County Medical Society February 21 were Drs. Franklin B. Cooper, Oakmont, Pa., on "Treatment of Pneumonia"; John G. Wurtz, "Thrombocytopenia"; Frederic S. Morris, "Internal Fixation for Fracture of the Femoral Neck," and Robert I. Baxmeier, "Gastroscopic Diagnosis."——Speakers before the Pittsburgh Academy of Medicine February 14 were Drs. John M. Lichty, on "Pericardial Effusions"; James O. Wallace, "Sclerosing Osteomyelitis," and Alexander H. Colwell, "Chronic Leukemia with Unusual Bone Lesions," a case report.

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SOUTH CAROLINA

Society News.—At a recent meeting of the Pee Dee Medical Association in Florence the guest speakers were Drs. Julian M. Ruffin, Durham, N. C., on pellagra and nicotinic acid; Madison Hines Roberts, Atlanta, otitis media and mastoiditis in general practice, and James J. Ravenel, Charleston, on prostatic calculi. ——Dr. Henry T. Chickering, New York, addressed the Columbia Medical Society January 9 on "Treatment of Pneumonia" and Dr. Francis E. Zemp, Columbia, on "Primary Jejunal Ulcer."

TENNESSEE

State Health Officer Reappointed.—Dr. Wilson C. Williams, assistant professor of preventive medicine and public health, Vanderbilt University School of Medicine, Nashville, was recently reappointed state health commissioner. Dr. Williams, after serving as health officer of Williamson County, took graduate work at the Johns Hopkins University School of Hygiene and Public Health. Afterward he joined the staff of the state department of health and was appointed commissioner in 1935. He has served under two previous governors. He graduated at Vanderbilt in 1925.

TEXAS

Personal. — Dr. Benjamin M. Primer, Austin, has been appointed director of the Travis County health unit to succeed Dr. Bolivar J. Lloyd, who resigned because of ill health.—— Mr. Justin F. Kimball, vice president of Baylor University in charge of the scientific schools and hospitals in Dallas, has resigned. Mr. Kimball was appointed to the Baylor position in 1929 after having served as superintendent of city schools in Dallas. In February 1938 he was honored at a dinner in recognition of his work in developing group hospitalization.

The Eleventh Annual Dallas Spring Conference.—The eleventh annual spring clinical conference of the Dallas Southern Clinical Society will be held March 13-16 with headquarters at the Hotel Adolphus. Each morning there will be general assemblies with addresses by guest speakers, followed except on Monday by graduate lectures presented by Dallas physicians. Luncheon periods will be devoted to round table discussions for different groups, with guest speakers present. Clinics will be conducted each afternoon at the hotel, and on Wednesday there will be in addition surgical clinics at Baylor, St. Paul, Parkland and Medical Arts hospitals. Monday evening there will be a smoker and Thursday evening the annual dinner with entertainment. Tuesday evening will be set aside for a clinicopathologic conference with the honor guests. Wednesday evening a symposium on diseases of the thyroid will be presented with Drs. Fuller Albright and Richard B. Cattell, Boston, and Louis J. Karnosh, Cleveland, as the speakers. The guests and the subjects they will discuss at the general assemblies are:

Dr. Albright, Medical Aspects of the Renal Stone Problem.
Dr. Cattell, Differential Diagnosis of Large Bowel Lesions.
Dr. Sanford R. Gifford, Chicago, Chronic Conjunctivitis.
Dr. Robert H. Herbst, Chicago, Importance of Early Recognition of Obstructions of the Bladder Neck.
Dr. Karnosh, Treatment of Simple Mental Depression.
Dr. Dean M. Lierle, Iowa City, Throat Manifestations of General Diseases.
Dr. Charles F. McKhann, Boston, Respiratory Diseases in Infants and Children.
Dr. William S. Middleton, Madison, Wis., Lymph Node Diseases: Their Differential Diagnosis and Treatment.
Dr. Harry E. Mock, Chicago, Physical Therapy—What It Is and What It Will Do.
Dr. Alfred C. Reed, San Francisco, Amebiasis.
Dr. Wendell G. Scott, St. Louis, Roentgenologic Methods Employed in the Diagnosis of Pulmonary Diseases.
Dr. Richard TeLinde, Baltimore, Office Gynecology.

There will be scientific and technical exhibits and a program of motion pictures. Dr. Robert A. Trumbull is president of the clinical society and Dr. W. Grady Reddick, director of clinics.

WASHINGTON

Society News.—A symposium on disease of the biliary tract was presented at a meeting of the King County Medical Society, Seattle, February 20, by Drs. Clyde R. Jensen, Thomas W. Blake, Charles E. Watts and John A. Duncan. Dr. Kenneth K. Sherwood discussed "Symptomatology of Atrophic Arthritis."——Drs. Willard F. Hollenbeck and Louis P. Gambee, both of Portland, addressed the Cowlitz County Medical Society, Longview, January 18, on "Liver Damage in Gallbladder Diseases" and "Surgery of the Gallbladder and Bile Ducts" respectively.

Group Hospitalization Approved.—The board of trustees of the Washington State Medical Association at a meeting in Seattle January 8 approved the principle of group hospitalization and recommended that county societies assume the duty of promoting such plans in their communities. The board disapproved, however, of a society's organizing a hospital plan as one of its functions. The committee that made a detailed study and submitted a report to the trustees was as follows: Drs. Caspar W. Sharples, chairman; Albert J. Bowles, Herbert E. Coe and E. Weldon Young, all of Seattle.

WISCONSIN

State Health Board Election. — Dr. William Webber Kelly, Green Bay, was elected president of the state board of health at a meeting in Madison January 6. Dr. Stephen Cahana, Milwaukee, was made vice president and Dr. Cornelius A. Harper, Madison, remains secretary and state health officer.

Bardeen Memorial Lecture. — Dr. Stephen W. Ranson, Chicago, delivered the Bardeen Memorial Lecture at the University of Wisconsin Medical School, Madison, February 28. His subject was "The Hypothalamus." Dr. Ranson is director of the Neurological Research Institute, Northwestern University Medical School, Chicago.

Society News.—At the annual meeting of the Milwaukee Society of Clinical Surgery January 24 the speakers were Drs. William J. Carson, retiring president, on "The Science of Surgery"; Karl F. Schlaepfer, incoming president, "Nupercaine Spinal Anesthesia in General Surgery," and Lucius W. Hipke, "Gastrectomy—Results in Ten Consecutive Cases Ten Years After Operation."

University Develops Cancer Research Facilities. — Research on cancer at the University of Wisconsin, Madison, is to be centralized in a new building now in process of construction. Funds amounting to about $240,000 have been provided for the building by a special bequest, by a contribution from the Wisconsin Alumni Research Foundation and a PWA grant of $108,000. It will be 102 feet long and 50 feet wide and will be connected with the Memorial Service Institutes of the university and Wisconsin General Hospital. Two floors will be devoted to biologic research, one to x-ray diagnosis and the first floor to radiologic research and treatment. The new building cannot offer space to all the university's work on cancer, which is being pursued in zoology, plant pathology, agricultural chemistry, physics, chemistry and various departments of the medical school, but it will have conference rooms and will serve as a clearing house to unify the varied activities, according to the *Wisconsin Medical Journal*. In the Wisconsin General Hospital cancer patients from all parts of the state are received, making all types of the disease accessible to research workers. The entire development is being directed by a graduate school committee consisting of Drs. William S. Middleton, dean of the medical school, chairman; Edwin B. Fred, Ph.D., dean of the graduate school and Michael F. Guyer, Ph.D., professor of zoology. Walter J. Meek, Ph.D., professor of physiology and associate dean of the medical school, is chairman of the building committee.

GENERAL

Society News.—At the annual meeting of the Federation of State Medical Boards of the United States in Chicago February 14 Dr. John R. Neal, Springfield, Ill., was made president-elect and Dr. Roy B. Harrison, New Orleans, became president. Dr. Frank M. Fuller, Keokuk, Iowa, was elected vice president and Dr. Walter L. Bierring, Des Moines, Iowa, reelected secretary.

Examinations in Anesthesiology. — Applications for the examination to be given April 8 by the American Board of Anesthesiology are now closed. Applications for the oral examination in St. Louis in May will be received until March 13. The next written examination will be held in various places September 9. The oral examination, part II, will be held in Philadelphia October 14-15. Application for this examination must be made by July 11 to the secretary, Dr. Paul M. Wood, 745 Fifth Avenue, New York.

Van Meter Prize Award.—The American Association for the Study of Goiter again offers the Van Meter Prize Award of $300 and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The award will be made at the annual meeting of the association in Cincinnati May 22-24, provided essays of sufficient merit are submitted. The essays may cover either clinical or research investigations, should not exceed 3,000

words in length, must be presented in English and must be typewritten, double spaced. A copy must reach the corresponding secretary, Dr. W. Blair Mosser, 133 Biddle Street, Kane, Pa., not later than April 15.

Grants for Research on Sex Problems.—Requests for aid from the National Research Council's committee for research in problems of sex and reproduction must be received before April 1, it is announced. In addition to a statement of the research to be undertaken, the committee desires information about the proposed method of attack, the auspices of investigation and the uses to be made of the sum requested. Preference will be given to proposals for the study of neurologic, psychobiologic and behavioral problems. Requests may be addressed to the chairman of the committee, Robert M. Yerkes, Ph.D., Yale University School of Medicine, New Haven, Conn.

LATIN AMERICA

Mexican Laboratory Named for U. S. Entomologist.—The National School of Biological Sciences of Mexico recently opened a new laboratory of entomology, which is named in honor of Dr. Leland O. Howard, chief of the U. S. Bureau of Entomology from 1894 to 1927 and principal entomologist of the U. S. Department of Agriculture from 1927 to 1931, when he retired. Dr. Howard was unable to be present at the ceremonies. Ambassador Josephus Daniels made an address in which he outlined Dr. Howard's career.

International Meetings This Year.—The Pan American Sanitary Bureau has issued a list of international meetings to be held in the Americas this year, including the following in Latin America:

Second Pan American Neuropsychiatric Week, Lima, Peru, March 20-28.
Fourth Latin American Congress of Odontology, Montevideo, March 12-19 (postponed from December 1938).
Eighth Pan American Child Congress, San Jose, Costa Rica, August 28 to September 4.
Intergovernmental conference of American countries on rural hygiene, Mexico City, toward the end of 1939 (postponed from Nov. 10, 1938).

FOREIGN

Society News.—The British College of Obstetricians and Gynaecologists will now be known as the Royal College of Obstetricians and Gynaecologists.——The fourth International Congress of Comparative Pathology will be held in Rome May 14-20, with sections devoted to human, veterinary and plant pathology.

Red Cross Health Committee.—The Advisory Health Committee of the League of Red Cross Societies held its second meeting at the headquarters of the league in Paris last October. The countries represented were Colombia, France, Germany, Great Britain, Guatemala, Italy, Japan, Latvia, Siam, Sweden, Yugoslavia and the United States. Dr. Hugh S. Cumming, former surgeon general of the U. S. Public Health Service, represented the United States. The principal subject discussed was the health of infants and preschool children in rural areas in the various countries.

Government Services

Annual Report of Food and Drug Administration

During the fiscal year ended June 30, 1938, the last complete year of enforcement for the Food and Drugs Act of 1906, the Food and Drug Administration of the Department of Agriculture sampled or inspected 68,125 shipments in interstate commerce and imports for possible violations of the law. On interstate samples 1,992 seizures were made and 726 prosecutions were begun.

Two major tragedies attributable to unsafe drugs occurred during the year, the deaths of more than 100 persons caused by "Elixir of Sulfanilamide" and twelve deaths from an alleged cancer serum contaminated with tetanus toxin. In a drive to remove the elixir from the market, the administration's agents accounted for 1,905 pints, 9 fluid ounces, which was 99.2 per cent of the entire amount manufactured. The data show that 93 pints, 6 fluid ounces reached consumers and about half of that amount was consumed. In the investigation of the cancer serum deaths the administration examined 111 10 cc. ampules. Forty-one of these bore the number of a lot which appeared to be the only one containing tetanus toxin; of these eighteen contained the toxin.

The administration made an extensive survey of rubber and membrane prophylactics against venereal disease and 181 consignments of these products labeled as useful in prevention of disease were seized when examination showed them to be defective. As a result, many producers withdrew stocks from the market and made drastic changes in manufacturing processes.

False claims on medicines accounted for criminal prosecutions against forty-five defendants and 117 seizures of the products of eighty-six shippers. Chemicals and preparations purporting to comply with the standards of the U. S. Pharmacopeia gave rise to forty-three seizures and prosecutions against thirteen manufacturers; the administration analyzed 2,072 samples, exclusive of ether. Of 2,916 cans of ether tested, 111 failed to meet the pharmacopeial standard. Criminal action was brought against one manufacturer for glandular products that did not meet the standard.

Totals of 1,564 samples of National Formulary chemicals and twenty-five glandular products were examined, resulting in criminal action against seven manufacturers.

Unofficial chemicals, including glandular products to the number of 2,757, the output of about 500 producers, were examined. Criminal prosecutions were instituted against nine manufacturers of unofficial chemicals and preparations and against three manufacturers of unofficial glandular products.

The administration's food activities included 297 seizures of fruits and vegetables for excessive spray residues, an increase over the previous year, due largely to crop increases, the report stated. In one state, however, certain growers sprayed their apples much later than was recommended and then refused to incur the cost of washing. As a result sixty-nine seizures were made of shipments from this state alone.

The problem of metallic contamination continued to be important. Two hundred and twenty-nine lots of imported sardines were examined and eighteen were refused entry because of the presence of excessive lead. A special campaign has been carried on with respect to maple products in an effort to induce producers to cease using lead-bearing equipment and utensils. Examination of 300 samples resulted in twenty-two seizures. Ninety-five import lots were examined, of which forty-one, amounting to 2,600,000 pounds, were refused entry. Although these operations were intended for the immediate protection of the consumer, they have had the effect of hastening fundamental corrections, the administration reported.

As a result of the "Elixir of Sulfanilamide" episode, attention was directed to the danger of use of diethylene glycol in flavoring extracts. In the course of a campaign 103 consignments of solvents and 104 shipments of flavors containing them were seized. Within a few months stocks of these solvents for food use and all food products containing them disappeared from the market.

More than 254,000 cans of cream for butter making were examined by state and federal forces, of which 6,957 were condemned. The salmon pack for 1937, amounting to about 7½ million cases, required no action, the report said. Twenty-seven lots of imported tuna, totaling 160,000 pounds, were detained, some because of lead and some because of decomposition. Of domestic tuna seven shipments were seized and one prosecution was instituted.

An important project of the year was a survey of the confectionery industry for the purpose of regulating certain manufacturers who rework and redistribute unfit stocks. Sanitary conditions were found to be deplorable in some factories, raw materials carelessly stored and objectionable; returned material was being reworked by some firms for cheap sale.

Of 379 plants examined, the majority were scrupulously clean, but seventy-eight small consignments, the product of thirty-eight manufacturers, were seized. Prosecution has already been recommended against five for shipping filthy candy and actions against others are in preparation.

Fines assessed by federal courts in food and drug cases under the statute ranged from as low as $4 to a maximum actually paid of $3,000.

The new Food, Drug and Cosmetic Act becomes completely effective next June 25. Sections designed to protect the consumer against dangerous drugs and cosmetics went into effect immediately on approval by the President June 25, 1938.

CORRECTION

Foreign Physicians Qualify for Licenses.—Under New York news February 25, page 755, THE JOURNAL stated that 622 of 1,063 foreign physicians who took the state medical examinations in January were successful. According to the New York *Times*, this figure appeared for the results of the state medical examinations for 1937-1938.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Feb. 4, 1939.

Traumatic Rupture of the Common Bile Duct

Uncomplicated rupture of the common bile duct due to injury must be a very rare condition. Mr. A. C. Lysaght observed at the Cardiff Royal Infirmary the following case, which he has reported in the *British Journal of Surgery*. A man aged 32, a steel erector, was struck in the back by a steel rafter weighing about 3 hundredweight, which was swinging on a crane, and was thrown forward on his stomach against a pile of steel girders. He felt excruciating pain and was taken to the hospital in an ambulance. On arrival, about an hour after the accident, he vomited undigested food, and he continued to do so. He was in severe abdominal pain; the legs were flexed, and there was boardlike rigidity of the abdominal muscles. There was bruising of the lower part of the back but none of the abdomen. The abdomen was exquisitely tender all over but especially in the right hypochondriac region. There was no dulness in the flanks, and dulness of the liver was present. The temperature was 96 F., the pulse rate 90 and the respiratory rate 18. Rupture of a viscus, probably the small intestine, was diagnosed.

The abdomen was opened, with the patient under spinal anesthesia supplemented by gas and oxygen, by a long paramedian incision to the right. The peritoneal cavity was full of bile-stained fluid. The small intestine showed no injury. The incision was enlarged upward for examination of the biliary organs. A small tear was found at the first and second parts of the duodenum, which was repaired. Morison's pouch was full of bile, which reaccumulated after emptying. This was found to exude from a minute opening in the free border of the foramen of Winslow. When this was enlarged it was found that the common bile duct was completely severed. The lower end of the duct could not be found; it apparently had retracted. Closure of the upper end of the common bile duct and anastomosis of the gallbladder with the stomach was performed. The abdomen was closed with drainage, and recovery was uninterrupted.

Sir Robert Philip

Sir Robert Philip, professor of tuberculosis in the University of Edinburgh and until recently chairman of the National Association for the Prevention of Tuberculosis, has died at the age of 81. He was the first to evolve a system for the open air treatment of tuberculosis in all stages from the teachings of Bodington, Brehmer and other pioneers. The disease had long been regarded as a deadly inheritance in certain families and under the name decline was a favorite cause of death of sentimental Victorian novelists. The treatment consisted in keeping the patient in one room with freedom from drafts, which were thought to be injurious. Then came Koch's discovery of the bacillus of tuberculosis. In 1888 Philip published in the *British Medical Journal* a paper entitled "A Contribution Toward the Etiology of Phthisis" in which he argued that, although the bacillus was the cause of the disease, clinicians had not a rational conception of the cause of death. He experimented on animals with sterilized tuberculous sputum, which proved to be very toxic. He was the first in this country to realize the importance of preventing infection, to investigate the conditions under which the families of the patients lived and to teach them how to avoid infection. In 1887 he founded the first tuberculosis dispensary in the world, holding that for every patient with diagnosed open tuberculosis there must be many infected contacts, who should be examined. Three years later Calmette founded a similar dispensary at Lille. Philip was the first in this country to realize the need for various coordinated institutions, the sanatorium, the farm colony, the open air school and the hospital for patients with advanced tuberculosis. The system became known as "the Edinburgh system." In 1890 he was awarded the Alvarenga prize of the College of Physicians of Philadelphia for an essay on pulmonary tuberculosis. In 1908 he attended the International Congress at Washington. Two years later he was asked what might be expected from a ten year program of operations proposed by a conference in Albany, N. Y. He wired in reply "Prosecute great program proposed, watch child as potential tuberculosis seedling, correct faulty compulsory environment and expect 40 per cent reduction by 1920 and practical disappearance within a generation and a half." In 1928 he received the Trudeau medal of the American Tuberculosis Association, given annually for the most meritorious contribution to the knowledge of tuberculosis.

PARIS

(From Our Regular Correspondent)

Jan. 28, 1939.

A Symposium on Pulmonary Embolism

Reference was made in a previous letter to the experimental study of the etiology and mechanism of pulmonary embolism by Prof. Maurice Villaret and his co-workers. They found that the size of the embolus is of far less importance in giving rise to sudden death than hitherto believed. Complete obstruction of a large pulmonary artery by a foreign body will not be followed by an immediately fatal result in animals, whereas the intravenous injection of finely pulverized pumice stone, 10 cc. per kilogram of the animal's weight, causes extensive and almost invariably fatal embolism. It appears that sudden death following occlusion of a small branch of the pulmonary artery is the result of a reflex set up by irritation of the vessel wall, which acts first on the respiratory and then on the cardiac centers.

At the November 30 meeting of the Société médicale des hôpitaux of Paris, pulmonary embolism in its experimental and clinical aspects was the subject of three papers. In the first, Prof. Villaret and his co-workers, after a brief summary of their experimental work, stated that recent studies by Leriche, Fontaine and Friedmann corroborated the observation that a neurovegetative reflex plays a very important part in embolism. Other investigators here had also confirmed the experimental work of Villaret and his associates. At present an effort is being made to determine whether there is a difference physiologically between the fatal reflexes which have their origin in the arterial zones and those which have their origin in the capillary zones. As to the mechanism of sudden death after embolism, it is not uniform, a fact which corresponds with the variation of the clinical pictures. With massive embolism, the mechanical obstruction of the circulation must be regarded as constituting the essential factor, but the factor of the neurovegetative reflex appears important to explain smaller embolisms.

PREVENTION OF EMBOLISM

The prevention of embolism presents less of a problem experimentally than the treatment. Brocq has shown that embolism can be prevented in rabbits by section of the vagus or of the sympathetic and in dogs by administration of atropine, ephredrine and sodium bicarbonate. Lesions such as congestion, hemorrhage or edema, so commonly observed in patients with pulmonary embolism, have been reproduced in animals by Delarue by various operations on the trunk of the vagus or sympathetic and on the cervical ganglions of the

latter. For prevention, experimentally the most effective drug is pressedrine (norephedrine sulfate) a constituent of pressyl (a mixture of camphramine and pressedrine), of which the blood pressure raising action is like that of the sympathetic. Atropine sulfate, alkalis such as sodium bicarbonate in 5 or 10 Gm. doses daily and papaverine all have a similar prophylactic action against embolism, but it is advisable to combine all these drugs, because patients present individual variations in their susceptibility toward drugs which act on the sympathetic and vagus. For the present, the authors advised giving only ephedrine, atropine and sodium bicarbonate to prevent postoperative pulmonary embolism, although some failures must be expected because patients differ greatly in their neurovegetative equilibrium.

NONOPERATIVE TREATMENT

The nonoperative treatment of pulmonary embolism can be summarized as follows: 1. If a syncope exists, begin immediately with artificial respiration and administration of oxygen. Inject relatively large doses of ephedrine, atropine, pressyl or pressedrine. 2. When there are severe anginal symptoms, preference is to be given to morphine, heroin and papaverine and, if necessary, atropine and anesthesia of the stellate ganglion. 3. To combat an asphyxia syndrome, papaverine in association with vasoconstrictors such as ephedrine or pressedrine should be given as well as respiratory stimulants and oxygen. 4. If the patient is in collapse, the drugs which act most rapidly are epinephrine, ephedrine and pressyl, associated with ouabaine and respiratory stimulants. 5. In cases of less severe pulmonary embolism, in which the chief symptoms are pain over the infarcted area, dyspnea and, later, dark blood-tinged expectoration, relatively large doses of morphine, heroin and papaverine are indicated.

BRONCHOSPASM

The second paper in the symposium, on bronchospasm associated with pulmonary embolism, was by the physiologist Prof. Leon Binet and Dr. Burstein. The authors employed a technic, referred to in a previous letter, in which the lung is isolated, regularly perfused and rhythmically aerated. With the aid of this technic, the reaction of the bronchi and pulmonary circulation to an embolism can be accurately recorded. When this isolated lung technic was employed, a marked rise was noted in the blood pressure proximal to the embolism and a decrease in the entire pulmonary blood volume. There is a complete absence of any bronchial reaction. In order to study the bronchial reaction it is better to use artificial respiration in animals. After an experimental pulmonary embolism under these conditions, a marked diminution in the caliber of the bronchi was observed, which is undoubtedly of reflex origin, as shown by the fact that when both vagi are divided or atropine is given before the experiment, a bronchospasm fails to take place after the embolism. Unquestionably the vagus is stimulated reflexly and gives rise to a constriction of the bronchi. This may explain the marked dyspnea in cases of pulmonary embolism.

GENUINE VS. PSEUDO EMBOLISM

The third paper, on genuine and pseudo pulmonary embolism, was by Dr. Pierre Ameuille and his co-workers, who said that in view of recent experimental work a revision of our former conception of pulmonary embolism is necessary. They criticized the method commonly employed at necropsy of searching for an embolus by opening the pulmonary artery in a centrifugal manner. If the clinical picture leads one to suspect the presence of an embolus, it is preferable to inject a solution of gelatin colored with carmine into the main right and left pulmonary arteries. The entire area supplied by the arteries is sharply outlined in red, whereas if an embolus is present it prevents the entrance of the colored gelatin and the area supplied by the blocked vessel appears as an unstained pale cone in the midst of an intensely red zone. By a search at the summit of this unstained conical area, the artery and its occluding clot can be easily found. If no embolism exists, the entire lung is stained red. This technic was employed in eight necropsies on patients who had died suddenly under conditions which led to suspicion of a pulmonary embolism, such as preexisting femoral thrombophlebitis or sudden death following an operation. An embolism was found in four of the eight cases. In one it was evidently of long standing, intimate adhesions existing between the wall of the vessel and the clot. The clinical history was of death after five minutes of subacute dyspnea, indicating an onset of symptoms several days after the pulmonary embolism. Similar old clot formations in the pulmonary circulation without clinical symptoms were noted in two of four cases of preexisting femoral thrombophlebitis.

The authors stated that cases are encountered in which, clinically, one would expect to find a pulmonary embolism at necropsy yet none is discoverable even with the technic they recommend.

These observations emphasize how unwise it is to expect much of a result from an embolectomy, because the clinical picture may be that of a pulmonary embolism yet no actual clot be demonstrated or, as recent experimental work shows, minute emboli may give rise to the same clinical picture as large ones.

BERLIN

(From Our Regular Correspondent)

Jan. 16, 1939.

Vitamin C Deficiency

It has been commonly assumed that a vitamin C deficiency leads to depletion of the general functional capacity. Precise information on this problem had been lacking until Dr. Lemmel of the medical policlinic of the university at Koenigsberg undertook a thorough investigation. In his report he states that some of the manifestations which are designated by the generic term spring fatigue are based on vitamin C deficiency. He conducted an experiment on 110 inmates of a home for deaf-mute children. During the winter of 1937-1938 the dietary of these children was relatively poor in vitamin C. Then one half of them began to receive a daily ration of ascorbic acid. The one group was regarded as satisfactorily supplied with vitamin C; the other group clearly presented a medium grade vitamin C deficiency. The two groups were undifferentiated as to general physical development and capability of resistance to cold. After four months of observation by the school head it was possible to evaluate the capabilities of the children. Those to whom additional vitamin C had been administered tended to show improvement, whereas those whose diet was deficient in vitamin C tended to show impaired capabilities. Furthermore, a broad parallel could be proved between the modification of capability and the amount of the vitamin C deficiency. This experiment demonstrates that vitamin C deficiency, though of medium grade, impairs normal health.

Training of Colonial Physicians

The national führer of physicians, Dr. Wagner, has announced that "in the event of a restoration of Germany's colonies" there will be a demand for doctors "who are in some measure specially prepared for colonial service." Care must be taken that this preparation shall follow a uniform plan under the supervisory cooperation of the national chamber of physicians. If the time comes when doctors are needed for colonial service, only those applicants will be considered who have taken a course of training authorized by the national chamber of physicians.

Prof. Albert Fraenkel Is Dead

Albert Fraenkel, whose name is indivisibly linked with strophanthin therapy, died in Heidelberg Dec. 22, 1938, aged 74. He was especially influenced during his student days at Munich by the physiologist Voit and later at Strasbourg by Recklinghausen and Kussmaul. On account of a pulmonary disorder Fraenkel spent much time in sanatoriums. He thus came to enter practice at Badenweiler, a health resort in the Black Forest. Years later, although he had changed his place of residence, he continued to be known as Fraenkel of Badenweiler. In 1906 he moved to Strasbourg and there laid the foundations of that intravenous strophanthin therapy which was his principal contribution to science. He founded after the war a middle class sanatorium known as Speyerershof, at Heidelberg. This model institution fulfilled a great need of the most worthy class of the German population, namely educated persons in modest circumstances. Here Fraenkel found the opportunity to test the intravenous use of strophanthin with a large number of patients. He established graduate courses at the Speyerershof, and his methods thus came to attain wide recognition in Germany. Later he made his work known abroad by lectures in Anglo-Saxon countries.

Fraenkel emphasized the social significance of medical activity. As he repeatedly said, the social milieu was to him the most telling factor in his consideration of patients. The Rohrbach hospital in Heidelberg, a well equipped sanatorium, was his creation. He was a kindly, well balanced person and an excellent physician of the highest scientific rank, one of those figures who contributed so richly to that international prestige of the German physician which endured for so many decades.

ITALY

(From Our Regular Correspondent)

Jan. 22, 1939.

Congress of Internal Medicine

The Società Italiana di Medicina Interna recently held its annual meeting at Rome. Professor Maragliano discussed preventive medicine with special reference to immunization. An early diagnosis can be made from the history of the patient and by a careful clinical examination. It is not necessary to wait for the development of precise clinical symptoms.

MYOPATHIES

Professors Meldolesi of Rome, Siedel of Munich and Putti of Bologna were official speakers on primary myopathies. They said that because the muscular pigment myoglobin is greatly reduced in primary myopathies the muscles look like pieces of fish. Knowledge of the nature and function of myoglobin has widened by the study of primary myopathy. Myoglobin is similar to hemoglobin. It binds bimolecular oxygen in the venous blood and induces an intramuscular storage of oxygen for the intracellular respiration of muscular tissues. It is formed in the muscular fibers from a factor which is a derivative of food proteins. The decrease in myoglobin in the muscles alters the metabolism of glusides, creatinine bodies, adenylpyrophosphoric acid and the derivatives of the last in the muscle. Consequently there is little utilization of these substances when administered to the patient. Primary myopathy is an organic hereditary disease. Endocrine and pancreatic digestive alterations are frequent. American physicians report curative results from aminoacetic acid.

Professors Siedel and Meldolesi spoke on the chemical properties of myobilin, which is a bile pigment. In the primary myopathies there is destruction of myoglobin with consequent formation of myobilin and increased elimination of bilirubinoid substances in the urine, which gives a positive fluorescent reaction. The elimination of fluorescent substances through the urine in some cases is 300 times as much as normal. Stereobilin, urobilin and myobilin are identifiable in the urine.

Professor Putti reported satisfactory results from myotenotomy or progressive functional correction and in twelve cases of primary myopathy. The treatment was followed by physical and reeducational exercises. The results two years after treatment are satisfactory.

THE MENOPAUSE

Professor Sebatini of Genoa University was speaker for the second official topic, the menopause. Whether the climacteric and the stopping of ovulation are due primarily to senile involution of the ovary and secondarily to a loss of the maturating functions of the structure from absence of hypophysial hormones in the aged, or the reverse, is still unknown. There is a tendency, however, to believe that the phenomena depend primarily on the ovary. The pathologic disturbances in the climacteric are due to either increased or diminished function of various endocrine glands. The intensity of the sympathetic and endocrine climacteric disorders depend on the constitution. Treatment with estrogenic substance attenuates the disturbances. The physiology of ovulation and menstruation simulates the constant movement of an uninterrupted chain. According to the speaker a true climacteric age in man does not exist. The phrase means either early senility or nervous exhaustion from syphilis, alcoholism or latent myocarditis.

ALTERATIONS IN ABDOMINAL ORGANS

The third official topic, associated syndromes of organs at the upper part of the abdomen, was discussed in common with the Società di Chirurgia, which held its meeting in Rome at this time. Professor Antognetti of Rome concluded that pathologic alterations of a given organ induce simultaneous changes in other structures which are in functional correlation with the involved organ. The physiologic relations of the upper abdominal organs can be considered from the (1) embryologic, (2) vascular and lymphatic, (3) humoral, (4) reflex nervous and nervous and (5) functional synergic correlations.

Professor Pende emphasized the importance of studying associated syndromes of organs of the upper part of the abdomen from the angle of functional correlations of the organs, especially the transverse colon, duodenum and jejunum, stomach, liver, cholecystic and extrahepatic bile ducts, kidneys, adrenals and celiac plexus, including the two vagi and splanchnic nerves and the epigastric segment of the aorta. The fulcrum of physiopathologic correlations of the structures is the balance of insulin and epinephrine secretions, which maintain the regulating neurochemism of the structures. The speaker differentiated the syndromes in seven different nosographic categories as they give predominant symptoms of (1) anemia and dysemia, (2) disturbances of the digestive tract, (3) metabolic and lithiasic disorders, (4) hemodynamic diseases, (5) excretory disorders, (6) dysfunction of the organic powers of defense and (7) neurocenesthopathy.

Marriages

JAMES LUCIUS DAVIS, Thacker Mines, W. Va., to Miss Katherine Longcor of Greendell, N. J., Nov. 19, 1938.

MARION HENRY BERTLING to Mrs. Eleanor Rice Baker, both of Rock Creek, Ohio, at Cortland, January 28.

WILLIAM FREDRIC DELP to Miss Dorothy Elizabeth Wallner, both of Pulaski, Va., Nov. 15, 1938.

DAVID GALE DUNCAN, Huntington, Ore., to Miss Miriam Puspanen of Portland, January 7.

BEATRICE TOMBLIN to Mr. Henry Grivi, both of Los Angeles, at Riverside, Calif., Dec. 31, 1938.

R. FORD RATLIFF, Lucedale, Miss., to Mrs. Nannie Walker Ratliff of Vancleave, January 25.

Deaths

John Douglas ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1898; clinical professor of surgery, New York University College of Medicine; member of the American Surgical Association; fellow of the American College of Surgeons; in 1917 chairman of the surgical section of the New York Academy of Medicine; past president of the New York Surgical Society and the Medical Society of the County of New York; served at various times on the staffs of St. Luke's Hospital, Bellevue Hospital, Knickerbocker Hospital, General Memorial and Harlem Eye and Ear Hospital; on the medical draft board during the World War; author of numerous papers and reports on surgical subjects; aged 63; died, Dec. 5, 1938, of heart disease.

James Wallace Esler ✠ Washington, D. C.; University of Pennsylvania School of Medicine, Philadelphia, 1920; professor of clinical cardiology, Georgetown University School of Medicine; formerly secretary of the Washington Heart Association; aged 44; on the staffs of the Garfield Memorial Hospital, Georgetown University Hospital, Central Dispensary and Emergency Hospital, where he died, Dec. 15, 1938, of carcinoma of the stomach.

Wrey Gilmor Farwell ✠ Medical Inspector, Commander, U. S. Navy, retired, Fort Lauderdale, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1904; fellow of the American College of Surgeons; served during the World War; entered the navy in 1904 and retired in 1925 for incapacity resulting from an incident of the service; aged 55; died in December 1938 of chronic myocarditis and coronary occlusion.

Andrew S. Gregg, Fayetteville, Ark.; St. Louis Medical College, 1881; member of the Arkansas Medical Society; past president of the Arkansas State Board of Health; past president of the Washington County Medical Society; health officer; fellow of the American College of Surgeons; on the staff of the Fayetteville City Hospital; aged 81; died, Nov. 21, 1938, of coronary thrombosis.

John Penny Kaster ✠ Topeka, Kan.; Rush Medical College, Chicago, 1881; fellow of the American College of Surgeons; chief surgeon, Atchison, Topeka and Santa Fe Railway Company and Hospital Association; aged 81; died, Dec. 13, 1938, in a hospital at Wichita, of arteriosclerosis and myocarditis with bundle branch block.

John Punton, Kansas City, Mo.; Miami Medical College, Cincinnati, 1883; member of the Missouri State Medical Association; at one time trustee and professor of nervous diseases, University Medical College of Kansas City; aged 85; died, Dec. 3, 1938, of coronary thrombosis and hypostatic pneumonia.

Benjamin Franklin Coe ✠ Indiana, Pa.; College of Physicians and Surgeons, Baltimore, 1895; fellow of the American College of Surgeons; member of the Radiological Society of North America; member and president of the staff of the Indiana Hospital; aged 66; died, Nov. 15, 1938, of heart disease.

I. Oto Schobl, Manila, P. I.; Universita Karlova Fakulta Lékařská Praha, 1904; at one time chief, division of biology, Bureau of Science; formerly associate professor of pathology and bacteriology, Temple University School of Medicine, Philadelphia; aged 61; died, Oct. 13, 1938, in Tokyo, Japan.

Lewis Stuart Johnston, San Antonio, Texas; Dallas Medical College, 1901; served during the World War; at one time acting assistant surgeon, U. S. Public Health Service; aged 63; died, Dec. 8, 1938, in El Paso, of sarcoma of the mesentery and pulmonary embolus following operation.

Irving Coburn MacDonald ✠ Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; aged 64; on the staff of St. Barnabas Hospital, where he died, Dec. 5, 1938, of cerebral embolism, cerebral hemorrhage and coronary thrombosis.

Edward Bowe ✠ Jacksonville, Ill.; Rush Medical College, Chicago, 1897; on the staffs of the Passavant Memorial Hospital and Our Savior's Hospital; former president and secretary of the Morgan County Medical Society; aged 65; died, Dec. 16, 1938, of myocarditis.

Max Baruch ✠ New York; Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg, Baden, Germany, 1909; on the staff of the Central and Neurological Hospital; aged 55; died, Dec. 13, 1938, of coronary thrombosis.

Edwin Bruce McDaniel, Cedar Rapids, Iowa; Rush Medical College, Chicago, 1900; veteran of the Spanish-American War; for many years a medical missionary; aged 65; died, Nov. 2, 1938, in Los Angeles.

John William Bowler ✠ Hanover, N. H.; Dartmouth Medical School, Hanover, 1906; for many years professor of physical education at Dartmouth College; aged 73; died, Dec. 27, 1938, of pneumonia.

Hunter Boyd Spencer, Lynchburg, Va.; University College of Medicine, Richmond, 1907; member of the Medical Society of Virginia and the American Roentgen Ray Society; aged 55; died, Nov. 12, 1938.

Robert White Barton, San Angelo, Texas; College of Physicians and Surgeons, Baltimore, 1884; aged 78; died, Dec. 20, 1938, in the Shannon West Texas Memorial Hospital of chronic myocarditis.

Walter C. Sims, Richland, Ga.; Atlanta Medical College, 1898; member of the Medical Association of Georgia; aged 66; died, Nov. 20, 1938, of peritonitis and injuries received in an automobile accident.

De Witt C. Greene, Buffalo; University of Buffalo School of Medicine, 1883; member of the Medical Society of the State of New York; aged 81; died, Nov. 25, 1938, of myocarditis and arteriosclerosis.

Joseph Conrad Pietroski, Cicero, Ill.; Chicago College of Medicine and Surgery, 1916; aged 49; died, Dec. 24, 1938, in St. Mary of Nazareth Hospital, Chicago, of coronary thrombosis.

Joseph Stannard Boynton, Santa Rosa, Calif.; University of Vermont College of Medicine, Burlington, 1884; aged 75; died, Nov. 11, 1938, of arteriosclerosis and chronic myocarditis.

Lewis N. Klove, Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; aged 66; died, Nov. 9, 1938, of hypertension and cerebral hemorrhage.

Oscar Barksdale ✠ West Memphis, Ark.; University of Tennessee College of Medicine, Memphis, 1914; served during the World War; aged 55; died, Dec. 18, 1938, of myocarditis.

John Charles Phillips, Wenham, Mass.; Harvard University Medical School, Boston, 1904; served during the World Ward; aged 62; died in November 1938 of heart disease.

Robert P. Dalton, Cape Girardeau, Mo.; Barnes Medical College, St. Louis, 1904; formerly member of the city board of health; aged 71; died, Dec. 18, 1938, of myocarditis.

Homer Isaac Keeney, San Francisco; Jefferson Medical College of Philadelphia, 1901; served during the World War; aged 62; died, Nov. 21, 1938, of coronary occlusion.

Adolph Faller ✠ Chicago; Chicago Medical School, 1918; on the associate staff of the Evangelical Hospital; aged 61; died, Dec. 3, 1938, of bronchopneumonia.

Hiram Milton Presler, San Diego, Calif.; Eclectic Medical Institute, Cincinnati, 1894; aged 73; died, Nov. 27, 1938, of hypertension and coronary occlusion.

Francis John Vincent Marx ✠ Westbury, N. Y.; University of Buffalo School of Medicine, 1923; aged 37; died in November 1938 in Phoenix, Ariz.

Charles Wesley Reed ✠ Irwin, Pa.; University of Kansas School of Medicine, Kansas City, 1932; aged 32; died, Nov. 23, 1938, in a hospital at Tulsa, Okla.

Thomas Calvin Kelly, Sidon, Miss.; Medical College of Alabama, Mobile, 1904; aged 63; died, Dec. 11, 1938, of hypertension and cerebral hemorrhage.

John Charles Quitmeyer, Chicago; Chicago College of Medicine and Surgery, 1915; aged 48; was killed, Dec. 2, 1938, when he was struck by a truck.

Aaron Denenholz, Brooklyn; New York University Medical College, 1897; on the staff of the Manhattan State Hospital; aged 63; died, Dec. 1, 1938.

William Hall Richardson, Milton, Ore.; St. Louis University School of Medicine, 1905; aged 59; died in November 1938 of bronchopneumonia.

Charles H. Griswold, Modesto, Calif.; Chicago Homeopathic Medical College, 1887; aged 77; died, Nov. 27, 1938, of carcinoma of the pancreas.

John Richard Lyon, Mount Pleasant, Ohio; Ohio Medical University, Columbus, 1895; aged 76; died, Nov. 21, 1938, of coronary thrombosis.

William S. Gibson, Burbank, Calif.; Eclectic Medical Institute, Cincinnati, 1882; aged 77; died, Nov. 8, 1938, of atrophic cirrhosis of the liver.

Walter Edward Williams, Olean, N. Y.; Jefferson Medical College of Philadelphia, 1904; aged 61; died, Nov. 18, 1938.

Thomas J. Irwin, Jellico, Tenn.; Chattanooga (Tenn.) Medical College, 1894; aged 70; died, Nov. 23, 1938.

John R. Vance, Stanton, Texas; Kentucky School of Medicine, Louisville, 1887; aged 82; died, Dec. 5, 1938.

Correspondence

"CLINICAL LABORATORIES AND THE AMERICAN CHEMICAL SOCIETY"

To the Editor:—The editorial "Clinical Laboratories and the American Chemical Society" in THE JOURNAL February 4 interests me. I infer that the work of clinical laboratories is "principally a commercial problem ancillary to the practice of medicine."

Undoubtedly this attitude fully explains why the American Hospital Association feels that the services of radiologists, physical therapists, anesthetists, cardiologists, pathologists and clinical pathologists should be included in group hospitalization projects, since, as has been stated in the journals of the hospital associations, these specialists cannot really be considered as practicing medicine, because they "merely carry out the orders of the practitioners of medicine, are subordinates, and assume no responsibility to the patient." Hence the term "ancillary" in the editorial sponsored by the American Medical Association strikes an ominously resonant note.

As a pathologist and clinical pathologist I find expression difficult under the circumstances. Having entered the field of pathology because I sought factual data relative to the mechanisms of disease, I have reaped a harvest of economic headaches which have only recently begun to clear up. Now I learn that I am in a line of work not only commercial but ancillary!

If pathology and clinical pathology do not constitute the practice of medicine—and some doubt seems to exist—then medicine could get along very well if physicians abandoned these specialties. Even now this branch is not overcrowded by those honestly interested in it as a career, and many definite trends are already seriously undermining the morale of those endeavoring to carry it on.

Chemists are capable of directing and developing the procedures of biochemical laboratories, and many of them possess sufficient clinical knowledge to permit certain biologic interpretations, but it seems quite illogical to assume that training in chemistry qualifies a person in hematology, serology, parasitology, clinical microscopy, bacteriology, and the miscellaneous diagnostic procedures of clinical pathology. Furthermore, it would be the height of absurdity for physicians to abandon pathologic anatomy to a chemist or any one without the necessary clinical training.

The situation in Pennsylvania is most interesting, especially when one realizes that Dr. I. D. Metzger has been the ardent exponent of his present point of view consistently for many years and that he has seldom received the support due him from the medical spokesmen of Philadelphia and of the state at large. It certainly behooves the learned profession of medicine to support him now.

The American Board of Pathology is now an accomplished fact and an integral unit of our national medical organization. By this board the specialties of pathologic anatomy and clinical pathology are clearly defined. Much work and a large field in the practice of medicine now belong to the certificated pathologist. There exist no other specialties that are not dependent on him to a very appreciable extent. His field, like that in other specialties, can be closely guarded to prevent exploitation.

Much of the present structure of modern scientific medicine is founded on the work of pathologists and clinical pathologists. We have only recently embarked on the development of our own American culture in these sciences which now analyze the mechanisms of disease. If they are turned over too completely to nonmedical personnel because we are somewhat dubious as to their status in the practice of medicine, such doubt might not long be entertained by the nonmedical group who take them over.

NORMAN W. ELTON, M.D., Buffalo.

SULFANILAMIDE IN THE PREVENTION OF PUERPERAL INFECTION

To the Editor:—May I call your attention to a probable error in the communication "Sulfanilamide in the Prevention of Puerperal Infection" from your Paris correspondent, THE JOURNAL, February 4, page 459.

In an abstract of Dr. Picot's thesis, appearing in the *Presse médicale* (**46**:1935 [Dec. 31] 1938), it is stated unequivocally that the drug used was not sulfanilamide but a derivative, *p*-benzylaminobenzenesulfonamide, commercially known as septazine. The title of this abstract reads: Guy Picot. Contribution à l'étude de la prophylaxie de l'infection puerpérale. Essai de chimiothérapie préventive (Benzyl-Amino-Benzène-Sulfamide) [Travail de la Clinique Tarnier].

JENNIE PINCHACK, New York.
Librarian, E. R. Squibb & Sons.

"ORCHITIS AFTER MUMPS"

To the Editor:—Anent "Orchitis After Mumps" (THE JOURNAL, January 14, p. 170), I reported a case (THE JOURNAL, Sept. 2, 1916, p. 741) in which I grafted a piece of testicle into remnants of such a lost testicle in the hope of at least restoring a masculine voice to a man who had lost it with his testicles. The effect of the graft restored the voice in a surprising way not by physical presence but because it stimulated remains of the destroyed testicle into nearly normal development. I showed the patient at a meeting of the New York Surgical Society and the case was held to be more important than my case of pregnancy after ovarian grafting, the latter a case in which the tissues of the receptor happened to be taken out of foreign tissue. Later I tried various experiments for instituting tolerance but failed in that quest; I hope some one will do it. In my eighties I am past all useful work with the exception of stories for the boys when they make welcome calls.

ROBERT T. MORRIS, M.D., Stamford, Conn.

A COMMENT ON BIOLOGICALLY CORRECT TRAFFIC EQUIPMENT

To the Editor:—A recent interesting note (Fabing, H. D.: A Neurologic Note on Traffic Lights, THE JOURNAL, Sept. 24, 1938, p. 1166) stressed the need for biologically, physiologically and psychologically sound technic for making our machine age civilization fit the human being who has to use and enjoy it. Quite rightly it was held that traffic is one of the important fields in which such technics are necessary. This principle can and should be applied to the various problems arising from traffic facilitation and control. It is unfortunate, however, that the article goes on to recommend as biologically sound a type of traffic signal which has been tried out and discarded.

The type of signal recommended was of the clock type in which a hand indicates how much time the red, yellow or green will remain showing. This type of signal and its variations have been discarded for several reasons, one of the chief being one of practical motorist psychology. That is, it has been found that when a motorist is given a warning that a light is about to change he tends either to "beat the light" or to "run through the yellow," depending on whether he is stopped or is moving. This is a psychologic feature to be avoided, since it results in collisions.

Avoidance of the difficulty was provided by the committee of traffic experts who drew up the Manual for Standard Traffic Control Devices (American Association of State Highway Officials and National Conference on Street and Highway Safety, Manual of Uniform Traffic Control Devices, Washington, D. C., 1937). The manual recommends a warning yellow only for the driver who is coming to a halt.

The author contended that the standard three color signal was hard on the nervous system and cited increased heart beat, sweating and other autonomic nervous signs of being under strain. Of course, such nervous tension may occur in varying degrees under various situations. A ball game, the approach of a pretty girl, lack of experience in handling a car and many other factors might produce similar results. Color blindness might make it difficult for a driver to distinguish between the red and the green signal and thus cause extra strain. If so, he would do well to note that the standard code places the red signal always at the top of the three signal lenses and to advocate adoption of the standard in all cities where this has not yet been accomplished.

Certainly this nervous reaction to the standard signal cannot be explained on the basis of Pavlov's "conditioned neurosis" experiments unless some special condition such as color blindness is present. Pavlov's studies were quoted quite correctly as producing "neurotic" behavior on the part of a dog trained to obtain food at one signal and avoid it at another. It should be noted, however, that the dog was first trained to widely different signals and then gradually the two opposite signals were made more and more alike or else the signals were alternated continuously and rapidly so as to be practically simultaneous from the dog's point of view. The "neurosis" occurred when the two signals became very similar; that is, when the animal was unable to distinguish them with any certainty. In other words, the task became too difficult for the animal to perform with his natural ability. This result has been investigated further and confirmed more recently by American investigators (Anderson, O. D., and Liddell, H. S.: Observations on Experimental Neurosis in Sheep, *Arch. Neurol. & Psychiat.* **34**:330-354 [Aug.] 1935. Liddell, H. S.: The Experimental Neurosis and the Problem of Mental Disorder, *Am. J. Psychiat.* **94**:1035-1043 [March] 1938).

Certainly the average motorist has no difficulty in distinguishing between the red and the green of the standard signal light at an ordinary intersection, nor are they alternated in such a fashion that he is unable to tell what he is being commanded to do. Thus, the comparison of the human response to the red and green signals with the animal's response to signals which were undistinguishable does not hold.

Now let us return to the possibility of color blindness. Color blindness is known to affect but a relatively small percentage of the population, but it is quite possible that the colors used in some of the lenses on the market could be improved for the benefit of the red-green blind person.

Otherwise it seems that the present three color traffic signals as recommended by the Manual of Standard Traffic Control Devices are fairly well suited to the psychologic and physiologic requirements of the ordinary driver.

On the other hand, the contention that traffic facilities and control devices must be psychophysiologically and psychologically fitted to the needs of the driver certainly should apply to all phases of traffic. This means that in the design and installation of such facilities and equipment it is necessary to consider the psychology and physiology of vision, of the ability to read signs, of human inertia, of fatigue, of muscular skill and manipulation, of distraction and attention and of the effect of uncertainty on the driver's reaction time.

For instance directional signs at highway intersections must be of such size, letter design and text organization as to be read by the motorist when he is still a long distance away. He thus will have time to make up his mind as to what he is going to do and be able to do it without sudden turns or stops and their attendant collisions and accidents.

Again, highway lighting should be of such adequacy either from headlights or from overhead lighting that the driver will be able to see and act quickly. It has been shown that any uncertainty of vision, whether from lighting or from other factors, reduces the speed of decision and action of the driver.

As another example, a clear view of the road ahead should be provided for a sufficient distance to allow safe passing and stopping at the speeds used on the highway. This means a distance which will allow time for perceiving and judging the speeds of oncoming cars, for passing the car ahead and for safe clearance at the end of the pass. Such passing distance, of course, cannot be provided at all points along the road, and at points where this is impossible the requirement should be for sufficient clear distance to give the driver time enough to execute a safe stop.

Strides toward all these objectives have been and are being made, although there is still much to be desired. I agree with Fabing that the goal is highly desirable, and efforts should be made to achieve it.

T. W. FORBES, PH.D., New Haven, Conn.
Bureau for Street Traffic Research.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

POISONING FROM AIRPLANE "DOPES"

To the Editor:—A patient works in an airplane factory where he is exposed to the fumes of airplane "dope." Does this "dope" give rise to any symptoms. If so, what symptoms? The patient gets better slowly after lieing off from work. C. W. BURGWIN, M.D., Guys Mills, Pa.

ANSWER.—During the period of the great war and for several years afterward one of the foremost industrial health problems centered about the chemical coating for fabric airplane wings. At that time poisonous materials were utilized. "Dope poisoning," an inelegant and medically undesirable term, was real, frequent and serious.

At the present time larger planes are almost uniformly provided with metal wings and other metal housings. Smaller planes, and particularly model planes and toys, make use of fabric wings and housing, so that "dopes" are still in some use. However, the chemical composition is changed, so that the earlier used toxic substances largely have disappeared. Lacquers are in wide use and these ordinarily contain various acetates, alcohols and toluene. Lacquer vapors are comparatively harmless, although the various acetates are minor respiratory irritants and toluene, if present, may lead to more extensive systemic damage. Toluene is in the series of coal tar hydrocarbons that includes benzene and xylene. Toluene is less dangerous than benzene, since it has a high boiling point and thus evaporates less freely. The action of toluene is somewhat similar to that of benzene and, if it has led to chronic involvement, blood changes may be expected, including anemia and leukopenia. This comment refers in general to lacquers such as are used on airplane fabrics, but in the present instance if any other "dope" than lacquer is utilized a special investigation of the particular product should be instituted.

References:

Young, Clifton A.: Dope Poisoning as a Potential Hazard in Spray Coating Airplane Wings, *U. S. Nav. M. Bull.* **31**: 63 (Jan.) 1933.
Smith, W. S.: Doping in Aircraft Works, Ann. Rep. Chief. Inspect. Factories and Workshops, Great Britain, for 1917, p. 18.

MALE HORMONE IN HYPERTENSION

To the Editor:—One of my patients asked me about the effect of injections of male sex hormones (testosterone propionate) as a treatment for arterial hypertension. He told me that some of his friends had used this kind of therapy successfully. What is your opinion?

MANFRED LANDSBERG, M.D., Cudahy, Wis.

ANSWER.—There are no recent American reports on the administration of testis hormones in hypertensive arterial disease. From Vienna Steinach and his co-workers (Steinach, E., Peczenic, O., and Kun, H.: *Wien. klin. Wchnschr.*, Jan. 28, 1937, and Feb. 4, 1937) report reduction of the systolic tension in thirty-one of forty-nine male patients treated with androsterone benzoate. Reductions of the diastolic tensions were negligible.

Greene (*Lancet* **2**:79 [July 9] 1938) reports that in twenty-one male patients between the ages of 58 and 77 there was no significant change in the arterial tension after long and liberal

administration of testosterone propionate. The "before and after" variation of the diastolic tensions averaged from 3 to 4 mm. Thus the literature appears to deny any useful place to the testis hormone in the management of hypertensive disease. This is to be expected, for there has been no evidence indicating that diminution of the testis hormone or hormones has any etiologic significance in hypertensive disease. The primary principal of therapy involves the removal or at least the amelioration of etiologic factors. These must be searched for; they vary in each individual case.

ERYTHROCYTE SEDIMENTATION IN CORONARY OCCLUSION

To the Editor:—In a case of coronary thrombosis, sedimentation rates taken during the week persistently show a fall of 2 mm. in forty-five minutes. The patient during this period has been on morphine medication. Would drug therapy, such as morphine, influence the sedimentation rate, or is it possible that the rate is not influenced in coronary thrombosis until from seven to ten days after the onset of the occlusion?

LEO KELLER, M.D., New York.

ANSWER.—While an increased erythrocyte sedimentation rate is a constant finding in coronary occlusion, it is not safe to say that a normal sedimentation rate is an impossibility. There are other conditions in which an increased sedimentation rate is almost constantly present (notably active tuberculosis) yet occasionally a normal sedimentation rate will be found. A considerable number of proved cases of coronary occlusion have been studied with especial reference to the sedimentation rate. Numerous observations were made in each case. These studies have shown an increased sedimentation rate in all proved cases of coronary occlusion at some time during the course of the disability. In some instances the increased rate first appeared toward the end of the second week. There is little likelihood that morphine would affect the sedimentation rate.

Recent publications dealing with this subject:

Shookhoff, Charles; Douglas, A. H., and Rabinowitz, M. A.: *Ann. Int. Med.* **9**: 1101 (Feb.) 1936.
Riseman, J. E. F., and Brown, M. G.: *Am. J. M. Sc.* **194**: 392 (Sept.) 1937.

STARCH IN GLUTEN BREAD—MIXTURES OF DIFFERENT TYPES OF INSULIN

To the Editor:—What is the amount of starch in ordinary gluten bread, as compared with ordinary white bread made of the standard flour? What would be the proportion, by weight or by volume, of gluten bread as compared to white wheat bread? Is there any objection to mixing various types of insulin, for instance as a combination of regular insulin with solution of zinc insulin crystals? I find that I may (not yet proved) get what I wish by a combination of 5 or 8 units of regular insulin with 15 or 18 units of the solution of zinc insulin crystals mentioned. I am striving to get a one hypo a day combination. I have tried all sorts of ways but seem now to be approaching success. This I do by using a single needle, which is used to give the small preliminary dose of regular insulin, which acts promptly and will be effective until the slower solution of zinc insulin can come into the battle. The zinc insulin solution reaches its maximum effect in about eight to nine hours. Protamine zinc insulin, while theoretically perfect for the one hypo a day, does not in my hands give that result. The daily dose is administered in the morning, around 7:30. Two needles are used. The first is left momentarily sticking in the flesh, while the second is used only to extract the required dose of zinc type insulin. The second needle is then removed, the syringe slipped into the first needle still in the flesh, and the dose injected slowly. We are told not to mix various types of insulin, but I can see no adequate logic in that admonition.

M.D., Pennsylvania.

ANSWER.—The usefulness of gluten breads and other so-called diabetic foods is limited, as described in the General Decision of the Council on Foods (THE JOURNAL, Feb. 11, 1933, p. 411). Gluten breads are not uniform. The average of several analyses of wheat gluten bread shows the carbohydrate to be 28.9 per cent or approximately 30 per cent in contrast to the average of analyses of wheat bread, which is 52.6 or approximately 53 per cent. From this one might conclude that the carbohydrate in gluten bread was about three-fifths that of wheat bread. The subject, however, is not quite so simple, because the wheat gluten bread averages 25 per cent protein in contrast to the average wheat bread, which contains 9.2 per cent protein. A diabetic patient may convert 58 per cent of the protein into carbohydrate. Consequently, out of 100 Gm. of gluten bread one would have $25 \times 58 = 14.5$ Gm. carbohydrate formed in contrast to $9.2 \times 58 = 5.3$ Gm. of carbohydrate derived from 100 Gm. of wheat bread. The content of fat in the two kinds is different. Wheat gluten averages 3.6 per cent of fat and wheat bread 1.3 per cent. However, only 10 per cent of carbohydrate would be formed out of fat.

In general it is safer to teach patients to use a standard wheat bread and if they do not employ scales they may be able to buy wheat bread which is either sliced or marked for slices so that each slice contains 30 Gm. (1 ounce) and in it would be found from 16 to 18 Gm. of carbohydrate according to whether one figures the carbohydrate alone or that derived from carbohydrate, protein and fat. The variation in carbohydrate in different makes of gluten breads is considerable.

Theoretically there would appear to be no reason why one should not use regular insulin, protamine zinc insulin and a solution of zinc insulin crystals together. While various attempts have been made to do this, such as the ingenious one described, it has usually not been found practical in the treatment of large groups of cases, because there are so many variables in the chemistry of insulin and the treatment of diabetes.

HAZARD FROM AMMONIA FUMES IN BEAUTY SHOP

To the Editor:—A patient has a cough, which for a short time was accompanied by hemoptysis. I have made the usual complete studies and am treating her with satisfactory results thus far. The diagnosis is fibroid phthisis. However, there is a question of occupational hazard involved. She owns a beauty shop. She states that she has been exposing herself to fumes of ammonia for more than ten years, in the process of permanent waving. She has noticed a tendency to cough whenever she is exposed to these fumes, and she states that the other operators also are disturbed by them. 1. Could this be an etiologic factor in any form of pulmonary disease? 2. What part might this play as a predisposing or aggravating factor in pulmonary disease? 3. Are there any precautionary measures which can be used to minimize these dangers?

M.D., West Virginia.

ANSWER.—1. In some permanent waving work, cloth pads wet with aqueous ammonia are wrapped about strands of hair and then enclosed in electrical heating units, which bring about evaporation of the liquid present and lead to artificial waving. This process lasts about fifteen minutes and it is the lot of many women to have coughed, sneezed, retched and shed tears as a result of this exposure to ammonia vapors—all in the quest of beauty. Naturally, beauty shop operators are more extensively exposed because of frequent repetition of the process. As little as 400 parts of ammonia vapor per million of air will cause immediate irritation of the throat, and 100 parts per million is the maximum that should be tolerated in prolonged exposure. On entering the respiratory tract ammonia immediately reacts with the tissue there present, but only superficially. Ammonia as such is not absorbed. High concentrations of ammonia lead to spasm of the glottis and are thus irrespirable. Lower, but still high, concentrations may lead to extensive damage along the respiratory tract, chiefly characterized by pulmonary edema. Action on the heart and respirations constitutes a reflex from local action along the respiratory tract. In connection with severe coughing, bloody mucus may be produced; but the direct causation of an extensive hemoptysis is most improbable.

2. It is well known that prolonged coughing aggravates almost any pulmonary disease, including tuberculosis. Hence it may be believed that long or frequent exposures to comparatively low concentrations of ammonia may aggravate many types of pulmonary disease.

3. The prevention of this injury is simple by elimination of this type of permanent waving. Other chemicals may be utilized for the same purpose, some at least of which are not injurious.

ACRODERMATITIS CHRONICA ATROPHICANS

To the Editor:—Please tell me the treatment for crodermatitis chronica atrophicans.

M.D., Ohio.

ANSWER.—The inquirer undoubtedly has reference to the entity called acrodermatitis chronica atrophicans. This is one of the idiopathic atrophies of the skin. It is a diffuse process and, as its name indicates, favors the extremities, particularly the extensor surfaces.

The essential cause of this atrophy is not known. Some believe that the atrophy is due to a trophoneurosis. Others feel that mechanical, chemical or thermal insults acting on a predisposed skin are at fault. Infections, particularly tuberculosis and syphilis, are blamed. Lastly, disturbance of the endocrine glands is supposed to underlie acrodermatitis atrophicans.

The skin should be protected from injury of exaggerated thermal changes, irritants of various kinds and trauma. Foci of infection should be sought and eradicated. Tuberculosis and syphilis if present should, of course, receive appropriate attention. The entire nervous system should be examined. Administration of thyroid or one of the other glandular substances or products can be considered if examination of the patient warrants it otherwise. Local emollient applications can be used such as borated cold cream, equal parts of hydrous wool fat and petrolatum, olive oil, and liquid petrolatum.

INGESTION OF SOAPS

To the Editor:—Please discuss for me the possible harmful effects following the ingestion of soap. Please furnish references to the literature.

M.D., Texas.

ANSWER.—Soaps are the salts of fatty acids and bases. The fatty acids of ordinary soaps are oleic, palmitic and stearic. They combine with bases to form soaps soluble or but slightly soluble in aqueous mediums. The soluble soaps are compounds of potassium and sodium, the less soluble are of magnesium and calcium. The harmful effects from the ingestion of solutions of the soluble soaps depend on the concentration, the amount of free alkali and the soap itself. Dilute solutions in small quantities are harmless. The harmful effects of solutions with appreciable amounts of free alkali are due mainly to the corrosive action of the base on the mucous membranes of the digestive system and, with aspiration, of the respiratory passages. Hartmann (according to Else Petri, Friedrich Henke and Otto Lubarsch: Handbuch der speciellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1930, vol. 10) concluded from experiments in animals with 0.5 per cent solutions of neutral potassium and sodium soaps that the necrosis and inflammation were due to the soap molecule, not alone to the alkali. The cause of sudden death from the ingestion of soap (Liebetrau: *M. Klin.* **2**:1228, 1906) is not clear, especially when the alkali content of the soap is small. Death of these patients has been ascribed to a generalized or blood toxic action, the latter in the sense of a hemolysis. The insoluble soaps in small quantities probably have no deleterious effects. The gastric secretions slowly convert the soap into free base and fatty acids (Hartsuch, P. J.: The Chemical Reaction Between Oleic Acid and Aqueous Solutions of Magnesium, *Arch. Path.* **25**:17 [Jan.] 1938). The effects of fat tissue hydrolysis and soap formation in the body is another problem (Hirsch, E. F.: Experimental Tissue Lesions with Mixtures of Human Fat, Soaps and Cholesterol, *ibid.* p. 35).

FAMILIAL NYSTAGMUS

To the Editor:—Recently, while examining a group of preschool children, I found two little girls of 5 and 6 (sisters) with a horizontal nystagmus. I could not elicit abnormalities of gait or tremors but all deep tendon reflexes were exaggerated. The mother says the children's father, their grandmother on the paternal side, two aunts on the paternal side and two first cousins about the same age have the same type of nystagmus. I have been unable to investigate the history except to ascertain that the father does have a horizontal nystagmus. Could you tell me whether there is a familial central nervous system lesion which could cause this? Are there similar histories on record? I should like to continue my investigation but wish to know whether it would be worth while and also wish I could have some idea as to diagnosis.

M.D., Wisconsin.

ANSWER.—There is a familial central nervous system disease known as spasmus nutans in which nystagmus occurs in children especially when the head is fixed. There may be a nodding movement of the head in association with the nystagmus as well as strabismus and blepharospasm. The condition was first described by Barton, Bennet and Newnham. All these increased movements may occur in children who come from a family with a history of neuropathic traits or diathesis. It would be well worth while to study the two cases as well as the family and report in detail. The condition is due, no doubt, to an inherited or a congenital instability of the nerve centers supplying these structures.

CUPREX FOR PEDICULOSIS

To the Editor:—What is your opinion on a preparation for exterminating "lice and nits," called Cuprex, put out by Merck & Company? Is there any advantage in using this over the older remedies? Are there any dangers attended by its use?

M.D., New York.

ANSWER.—Apparently the composition of Cuprex has not always been described in the same manner. It is described in Merck's Index (1930) as "a solution of a copper compound in organic solvents—clear, pale green, inflammable liquid." According to Bresslau (*Ber. Ges. Physiol. exper. Pharmakol.* **32**:912, *Chemical Abstracts*, 1926, p. 2223) Cuprex is a solution of copper salts of fatty acids. Schnellbach (*Schweiz. Apoth. Ztg.* **64**:91; *Chemical Abstracts*, 1926, p. 2391) states that Cuprex is a solution of copper abietate in a mixture of benzene and paraffin oil. The most recent statement of the composition of Cuprex is the following, received from the manufacturer in November 1937: "liquid petrolatum 20 parts, tetralin (tetrahydronaphthaline) 12 parts, acetone 6 parts, and copper oleate 'fraction of a per cent.'"

Merck & Co. call attention to the inflammability of Cuprex and to the general irritant properties of all pediculicides, which render their use for more than one or two applications inadvisable.

Although Cuprex has been marketed in this country for more than ten years, the files of the Council on Pharmacy and Chemistry, as well as the files of other available sources, reveal no published papers dealing with the comparative value of this preparation and other commonly used pediculicides.

Much information concerning various methods employed in the eradication of dermal parasites may be found in the special articles published in THE JOURNAL Oct. 3, 1936, page 1126, and Feb. 13, 1937, page 553. An interesting chapter on the treatment of pediculosis may also be found in the Handbook of Therapy.

HEAD SHAVING AND HAIR GROWTH

To the Editor:—Have you any information regarding whether or not by keeping the hair shaved from a baby's head for a period of twelve months or more the hair finally allowed to grow will be heavier in texture?

ARTHUR L. RICHARDSON, M.D., Pasadena, Calif.

ANSWER.—There is no evidence that shaving causes hair to grow more thickly or changes in any way the texture of the hair. The only effect is that of moderate stimulation of the scalp, which benefits hair growth.

BENZIDINE TEST FOR BLOOD

To the Editor:—What reaction takes place and what is the name of the blue product formed when benzidine and barium peroxide in diacetic acid (50 per cent) give a positive test for occult blood in the stool?

RAYMOND H. GOODALE, M.D., Worcester, Mass.

ANSWER.—The benzidine test for blood involves the oxidation of benzidine to a colored compound or mixture of compounds of unknown structure as the result of the combined action of peroxide and the iron in the hemoglobin. To eliminate the error from a positive test by other iron compounds, it is best to make the following modification: Add 2 cc. of glacial acetic acid to 5 cc. of the feces suspension and allow the mixture to digest at room temperature for from fifteen to thirty minutes; strain or filter and shake the filtrate with 5 cc. of ether. Separate the ether layer and apply the benzidine test, preferably by adding 2 cc. of a freshly prepared saturated solution of benzidine in glacial acetic acid to the ether solution plus 0.5 cc. of solution of hydrogen peroxide U. S. P. Mix well. Development of a blue appearance in from two to three minutes is a positive test for blood due to the hematin extracted by the ether.

CARBON TETRACHLORIDE

To the Editor:—I should like to ask you to publish a correction to a statement made in your July 30, 1938, issue. The first query on page 469 with your answer has just been brought to my attention. In speaking of the use of carbon tetrachloride extinguishers you state, in the third paragraph of your answer, that "Its vapors in concentrations above 100 parts per million of air may produce damage. When the concentration reaches 1,000 parts per million, immediate injury is in prospect for persons who may breath this vapor even for a few breaths." If you will refer to my article in THE JOURNAL for Nov. 21, 1936, under "Comments and Conclusions," page 1686, you will see that "it is concluded that 100 parts per million of carbon tetrachloride is a safe working concentration for continuous exposure of workmen during the working day (eight hours a day, five days a week). . . . Concentrations considerably higher than 100 parts per million are safe for short periods. It is believed that 1,000 parts per million is a safe peak concentration for half an hour a day (probably much longer than the user of a fire extinguisher would be exposed), with an average of 100 parts per million during the rest of the day." I agree with your last paragraph, in which you state that although these extinguishers may be theoretically dangerous they rarely lead to an accident. Your advice to use the extinguisher as quickly as possible and then to leave the area is a good one, but not because of the danger of phosgene alone. Under the conditions in which phosgene would be formed (great heat, metal surface, closed space) there is likely to be at least as great a hazard from carbon monoxide poisoning, which would be present regardless of the method used to combat the fire.

HENRY FIELD SMYTH, M.D., DR.P.H., Philadelphia.

VAGINAL ABSORPTION

To the Editor:—In the January 14 issue of THE JOURNAL on page 173, under Queries and Minor Notes, under the heading "Absorption from Vaginal Mucosa and Uterus," the answer states that "there is no absorption from the intact vaginal mucosa . . ." This statement is not quite correct, since it is known that the intact vaginal mucosa absorbs many substances. For example, vaginal suppositories containing estrogenic substance are constantly used, and many other substances are known to be easily absorbed through the vagina. It is quite possible that toxins from bacteria are absorbed through the same route, just as they are from other mucous membranes.

WILLIAM WOLF, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ARIZONA: *Basic Science.* Tucson, March 21. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson. *Medical.* Phoenix, April 11-12. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: *Medical (Regular).* Little Rock, June 8-9. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, 317 State Line, Texarkana. *Medical (Eclectic).* Little Rock, June 8-9. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written examinations.* San Francisco, July 10-13, and Sacramento, Oct. 16-19. *Oral examinations* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), San Francisco, March 22, Los Angeles, August 7, and San Francisco, Nov. 15. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, April 5-7. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Medical (Regular).* Hartford, March 14-15. *Endorsement.* Hartford, March 28. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Medical (Homeopathic).* Derby, March 14. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, June 26-27. *Medical.* Washington, July 10-11. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, June 19-20. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Joint Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, April 10-13. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

IDAHO: Boise, April 4-7. Address, Dir., Bureau of Occupational License, Rm. 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, April 11-13, June 20-22, and Oct. 17-19. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science.* Des Moines, April 11. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, State Department of Health, Capitol Bldg., Des Moines.

KANSAS: Kansas City, June 20-21. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: Louisville, June 7-9. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

MAINE: Portland, March 14-15. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical (Regular).* Baltimore, June 20-23. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Homeopathic).* Baltimore, June 20-21. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, March 14-16. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: Ann Arbor and Detroit, June 14-16. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, April 4-5. Sec., J. Chamler McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, April 18-20. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: Jackson, June. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: Helena, April 4-5. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science.* Omaha, May 2-3. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEW HAMPSHIRE: Concord, March 9-10. Sec., Board of Registration in Medicine, Dr. Fred L. Tow, State House, Concord.

NEW JERSEY: Trenton, June 20-21. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York, and Syracuse, June. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Building, State Education Department, Albany.

NORTH CAROLINA: Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, July 5-8. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: *Basic Science.* Oklahoma City, May 15. Sec. of State, Hon. C. C. Childress, State Capitol, Oklahoma City. *Medical.* Oklahoma City, June 14. Sec., Dr. James D. Osborn, Jr., Frederick.

OREGON: *Basic Science.* Corvallis, July 8, and Portland, Oct. 28. Sec. State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia and Pittsburgh, July. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

PUERTO RICO: San Juan, March 7. Sec., Dr. O. Costa Mandry, Department of Health, San Juan.

RHODE ISLAND: Providence, April 6-7. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 27. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Rapid City, July 18-19. Director, Medical Licensure, Dr. G. J. Van Heuveln, State Board of Health, Pierre.

VIRGINIA: Richmond, June 21-23. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WEST VIRGINIA: Charleston, March 6-8. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: *Basic Science:* Madison, April 1. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. *Medical.* Milwaukee, June 27-30. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, February 25, page 767.

Montana October Report

Dr. S. A. Cooney, secretary, Montana State Board of Medical Examiners, reports the written examination held at Helena, Oct. 4-5, 1938. The examination covered ten subjects. An average of 75 per cent was required to pass. Six candidates were examined, all of whom passed. Eighteen physicians were licensed by reciprocity and five physicians were licensed by endorsement. The following schools were represented:

PASSED		
School	Year Grad.	Per Cent
College of Medical Evangelists	(1938)	88.1
Loyola University School of Medicine	(1929)	82.9
Northwestern University Medical School	(1937)	86.2
Rush Medical College	(1936)	82.9
University of Illinois College of Medicine	(1938)	87.2
University of Minnesota Medical School	(1938)	81.8

LICENSED BY RECIPROCITY		
School	Year Grad.	Reciprocity with
Georgetown University School of Medicine	(1929)	Puerto Rico
Loyola University School of Medicine	(1937)	Ohio
Northwestern University Medical School	(1914)	Kansas
University of Illinois College of Medicine	(1935)	Minnesota
State Univ. of Iowa College of Med. (1930), (1934), (1937)		Iowa
Medical School of Maine	(1910)	Maine
University of Minnesota Medical School	(1924), (1937)	Minnesota
Washington University School of Medicine	(1924)	Wisconsin, (1936) Missouri
University of Nebraska College of Medicine	(1926), (1932)	Nebraska
Cornell University Medical College	(1937)	Oregon
Medical College of Virginia	(1936)	W. Virginia
Marquette University School of Medicine	(1933)	Wisconsin
Medizinische Fakultät der Universität Wien	(1934)	N. Dakota

LICENSED BY ENDORSEMENT		
School	Year Grad.	Endorsement of
College of Medical Evangelists	(1937, 2)	N. B. M. Ex.
University of Kansas School of Medicine	(1937)	N. B. M. Ex.
University of Minnesota Medical School	(1937)	N. B. M. Ex.
Cornell University Medical College	(1933)	N. B. M. Ex.

Iowa December Examination

Mr. H. W. Grefe, director, Division of Licensure and Registration, reports the written examination held by the Iowa State Board of Medical Examiners at Des Moines, Dec. 1-3, 1938. The examination covered eight subjects and included 100 questions. An average of 75 per cent was required to pass. Eighteen candidates were examined, seventeen of whom passed and one failed. The following schools were represented:

PASSED		
School	Year Grad.	Per Cent
Loyola University School of Medicine	(1938)	89.5*
Northwestern University Medical School	(1938)	82.4
Rush Medical College	(1937)	80.9,* 87.9*
School of Medicine, Division of Biological Sciences	(1937)	92.5*
State University of Iowa College of Medicine	(1938)	79.3,* 80.6,* 82.8,* 83.1,* 84,* 85.9*
Washington University School of Medicine	(1937)	80.5*
University of Alberta Faculty of Medicine	(1937)	81.6*
Medizinische Fakultät der Universität Wien	(1926)	85.1*
Ludwig-Maximilians-Universität Medizinische Fakultät, München	(1936)	81.1*
Universität Rostock Medizinische Fakultät	(1934)	81.5*
Universität Bern Medizinische Fakultät	(1937)	89*

FAILED		
School	Year Grad.	Per Cent
Rush Medical College	(1937)	75.1†

Eight physicians were licensed by reciprocity and one physician was licensed by endorsement from October 28 through December 10. The following schools were represented:

LICENSED BY RECIPROCITY		
School	Year Grad.	Reciprocity with
Atlanta Medical College	(1915)	Georgia
Rush Medical College	(1937)	Washington
School of Med. of the Division of Biological Sciences	(1937)	Missouri
Creighton University School of Medicine	(1926), (1935)	Nebraska
University of Nebraska College of Medicine	(1936)	Nebraska
University of Buffalo School of Medicine	(1937)	New York
University of Wisconsin Medical School	(1933)	Wisconsin

LICENSED BY ENDORSEMENT		
School	Year Grad.	Endorsement of
University of Pennsylvania School of Medicine	(1933)	N. B. M. Ex.

* License withheld pending completion of internship.
† Failed in physiology only.

Book Notices

Research in Mental Hospitals: A Survey and Tentative Appraisal of Research Activities, Facilities and Possibilities in State Hospitals and Other Tax-Supported Institutions for the Mentally Ill and Defective in the United States. Conducted by the National Committee for Mental Hygiene 1936-1937. Paper. Pp. 151. New York City, 1938.

By information collected through questionnaires, personal interviews and visits, a survey was made of existing facilities for research in mental problems in private hospitals and public institutions. This book constitutes an appraisal of that review. It was found that twenty of the 273 public institutions could be designated as research centers because of the character and quality of their investigatory work, the caliber of their personnel and the resources at their disposal for scientific study. In addition there are thirty-two public-supported hospitals that offer distinct possibilities for research work. Furthermore the report estimates that there are 150 of the 1,700 staff physicians in the public mental institutions of the country who show a definite interest in and ability for investigative work. The survey furnishes tangible evidence that a creditable beginning has been made in the development of research in public institutions and that further desirable expansion might be fostered with moderate encouragement and financial support. The extension of research, the report concludes, will be dependent in large measure on the availability of men with eager and inquiring minds who possess the qualifications for exploratory endeavor. In other words, many institutions can be encouraged to devote further efforts to psychiatric research, but the most important method of extending desirable investigative studies appears to be by encouraging recent graduates in medicine whose records would indicate promising careers in psychiatric research to enter this field.

Cranio-Cerebral Injuries: Their Diagnosis and Treatment. By Donald Munro, A.B., M.D., F.A.C.S., Surgeon in Chief for Neurological Surgery at the Boston City Hospital, Boston. Cloth. Price, $4. Pp. 412, with 62 illustrations. New York, Toronto & London: Oxford University Press, 1938.

The increasing number of head injuries resulting from automobile accidents in all sections of the country has forced on almost every practitioner of medicine the necessity of treating them. The treatment of craniocerebral injuries has passed through several stages of development and as a result many conflicting hypotheses based on erroneous observation have been advanced. For that reason Munro's book fills a much needed place in a medical library, a book to which the physician can refer for specific information concerning the most efficient methods of dealing with craniocerebral injuries. In the introduction Munro calls attention to the fact that the approximate number of fractured skulls in 1932 was 112,000. Unquestionably this number must be increasing and therefore the impracticability of expecting the few neurosurgical clinics of this country to care adequately for so many seriously injured patients is apparent. Munro is of the opinion that the problem of craniocerebral injury belongs to the general surgeon and that the neurologist and neurosurgeon should be consulted in the more complicated cases. This, of course, places a great responsibility on the general surgeon and makes it imperative that he acquaint himself with the most effective methods of treatment and provide himself with the necessary hospital and staff equipment. In this book an endeavor is made to present the information necessary for the general surgeon who either elects or is forced to treat craniocerebral injuries. It implies neither specialized knowledge nor technical skill. It has proved its worth in practice over a number of years and in a large active traumatic clinic. The book is based on experiences accumulated by all members of the staff, from house officers and residents to the chief of the service, and the methods that it describes have been equally effective in the treatment of patients suffering from craniocerebral injuries whether used by the most recent newcomer to the hospital or by any of his seniors. As a background for his discussion of the problem the author first elaborates on the fundamental cerebral physiopathology and then proceeds to the importance of history and examination of the patient. A chapter on roentgenology precedes the chapters on general principles of treatment, which are followed by chapters on special nonoperative and operative methods of treatment. Chapters on the nonoperable and operable groups of craniocerebral injuries are followed by a discussion of the complications due to necessary treatment and a most important chapter on convalescent care. A chapter on craniocerebral injuries of the newborn is a valuable addition to the general discussion. The final chapters, on first aid in craniocerebral injuries and the mortality and morbidity statistics with illustrative cases, complete this most interesting and valuable book. The volume should be in the library of every physician who attempts either by choice or by necessity to treat injuries of the head, for it makes a working knowledge of this subject available in a simple and comprehensive form.

The Medical Applications of the Short Wave Current. By William Bierman, M.D., Attending Physical Therapist, Mount Sinai Hospital, New York City. Including a Discussion of Its Physical and Technical Aspects. By Myron M. Schwarzschild, M.A., Physicist, Beth Israel Hospital, New York City. Cloth. Price, $5. Pp. 379, with 85 illustrations, including 25 plates. Baltimore: William Wood & Company, 1938.

There has been much unjustified and largely commercially inspired enthusiasm about the alleged specific therapeutic value of short wave diathermy. This volume is the well directed result of the combined efforts of a competent physical therapist and a physicist with special interest in medical electricity for a critical and broad portrayal of the present status of this new physical therapeutic agent. A short introductory chapter on the history of high frequency therapy is followed by 102 pages of scholarly and exhaustive discussion by Schwarzschild of its physical and technical aspects. In the chapter on physiologic responses Bierman takes the same stand as other conservative observers, that the primary action of the current is essentially due to the heat developed and that so-called nonthermal or specific effects are still to be proved. There is a large and fairly well illustrated chapter on technic. The final and largest chapter deals with clinical application, giving a comprehensive summary of the uses of short wave diathermy along the entire realm of pathology based on the author's own experience as well as on reports in the international literature. Bierman's special field of research, fever therapy by means of short waves, receives exhaustive attention in this and in the preceding chapters. Students of physical therapy and interested clinicians will find an unbiased and large store of information in this excellent volume.

New Jersey Formulary (N. J. F.). Compiled and Published by the Joint Committee on Professional Relations Consisting of the Committee on Pharmaceutical Problems of the Medical Society of New Jersey and the Committee on Professional Relations of the New Jersey Pharmaceutical Association. Chester I. Ulmer, M.D., Chairman, Robert P. Fischelis, Phar.D., Editor. Third edition. Paper. Pp. 64. Trenton, New Jersey, 1939.

This booklet opens with suggestions to physicians which include a plea for prescription writing in place of the prescribing of controlled-name products. This section includes the statement that "to combat commercial domination of therapeutics, the Council on Pharmacy and Chemistry of the American Medical Association was formed. Physicians should avail themselves of the help which their own Council can give them." The booklet contains the usual tables of weights, measures and equivalents and then suggests various preparations which are designated "N. J. F." (New Jersey Formulary). These are essentially modifications of the National Formulary preparations included in the book. Typical prescriptions are given for sedatives, elixirs, analgesic capsules, tonics and carminatives. The general purpose of this book is excellent. The advisability of suggesting prescriptions to physicians has certain advantages and also certain disadvantages. One item which is obviously designed to supplant expensive proprietary preparations of this type is a baby oil, "Olei Infantilis, N. J. F.," which contains 12.5 per cent of olive oil in light liquid petrolatum, with 1 part in 500 of the antiseptic chlorthymol, and oil of rose to perfume. On the whole, this booklet appears to be as useful as similar formularies which are on the market. It is especially designed,

however, for use in New Jersey, since it contains the "N. J. F." preparations which those in other states would not be familiar with. The idea of pharmacists and physicians cooperating in the preparation of such a book is preferable to the plan used in one other state of issuing such information from a joint committee of the Pharmaceutical Association and the Retail Duggists Association.

Diseases of the Ear, Nose and Throat. By Francis L. Lederer, B.Sc., M.D., F.A.C.S., Professor and Head of the Department of Laryngology, Rhinology and Otology, University of Illinois College of Medicine, Chicago. Fabrikold. Price, $10. Pp. 835, with 457 illustrations, including 16 color plates. Philadelphia: F. A. Davis Company, 1938.

To the available American textbooks in the field of otolaryngology may now be added a fine contribution by Dr. Francis L. Lederer of the University of Illinois College of Medicine. The textbook mechanically presents several features not available in other works, including excellent illustrations and innumerable black and white pictures, arrangement in two columns for easy reading, presentation in simple outline form, which is a great aid to the medical student, and the collaboration of specialists in many of the chapters, which provides exceptional authenticity. Each of the sections is prefaced by a compact consideration of the special anatomy concerned. The diseases are considered in the classic oslerian form of definition, etiology, bacteriology, transmission, epidemiology, symptoms, prophylaxis and treatment. There are no references to bibliography or to individual authorities, the author taking full responsibility throughout for the statements that are made, except for the recognition given in the preface. Perhaps for the medical student this is an ideal form. The index is detailed and exceedingly useful. The methods of treatment follow those generally accepted as established. Special recognition should be given to the pupils of Mr. Tom Jones, whose contributions to the illustrations are unique.

Dr. Ida: India. The Life Story of Ida S. Scudder, M.D., B.Sc., F.A.C.S., K.I.H., President, Medical College for Women, Vellore, India. By Mary Pauline Jeffery, M.D. Cloth. Price, $2. Pp. 212, with 19 illustrations. New York, London & Edinburgh: Fleming H. Revell Company, 1938.

American physicians who are inclined to feel pessimistic should read this story of their valiant colleague in Vellore, India. Dr. Ida Scudder, daughter and granddaughter of medical missionaries, decided there had been enough Scudders on the mission field and she was going to remain in America after her schooling was finished. Even when her mother became ill and she had to return to India to assist her father in the mission in remote Tindavanum she went as a short-term missionary. It was while there that she experienced the heart-breaking experience which changed the course of her life. Three times in one night she heard Indian men refuse her father's services for their child wives in desperate labor, and the next morning she watched the funerals of the three girls as they passed the Scudder home. It was after a day of "much thought and prayer" that she made her decision to study medicine that she might help Indian women. Years later, Jan. 1, 1900, she landed again in India, bringing with her $10,000 for the building of a hospital for women. While that first hospital was being built Dr. Ida found her hands full, fighting the black death, then cholera and leprosy and other afflictions of the Orient. Through the years that have followed, disease has been only one of her enemies. She has had to battle the shocking worship of the goddess Kali, the ignorance of charm doctors and the traditional system of medicine known as Ayurdedic, child marriage with its accompaniment of immature motherhood, and the caste system with its scorn of 45,000,000 Untouchables. Through her influence sanatoriums for the tuberculous have been established, a school for nurses started, dispensaries opened, hospitals built, and at last the Women's Medical College in Vellore. A children's home has been cared for by Dr. Ida herself with two of her colleagues. From a lovely, mischievous girl, Dr. Ida Scudder has developed into a poised and understanding woman, quite unspoiled by the praise and admiration accorded her by men and women from all parts of the globe. A tireless woman, always alert to help Indian women to help themselves. The book is interestingly written, not without humor. It should be worth reading from either the medical or the missionary point of view.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Issuance of Fictitious Diplomas and Licenses to Practice Medicine and Chiropractic as Scheme to Defraud.—The appellants were convicted under an indictment charging the use of the mails for the purpose of executing a scheme to defraud and appealed to the United States circuit court of appeals, eighth circuit.

In addition to the appellants, five other persons were named defendants in the indictment, but the record does not show what disposition was made of the charges against these other defendants. The indictment alleged in substance that the defendants named therein obtained, prepared and issued to numerous persons fraudulent and fictitious medical and chiropractic diplomas and certificates and fictitious licenses to practice medicine and chiropractic.

The evidence showed that appellant Alexander was secretary of the Eclectic Medical University at Kansas City, Mo., from 1910 to 1915. That school went out of existence in 1916 and was succeeded by the Kansas City College of Medicine and Surgery. The latter college went out of existence in 1926 and was in turn succeeded by the American Medical University. Alexander was custodian of and had in his possession the records of these institutions. Numerous fictitious medical diplomas introduced in evidence came from these schools and were issued by Alexander. The diplomas, dating back many years, were issued after the schools had gone out of existence to applicants who never attended the schools. One of the defendants, Laws, was secretary of the Eclectic State Medical Board of Arkansas from 1924 to 1933. He issued many fictitious licenses to practice medicine in that state to applicants, most of whom did not pass any examination. Another defendant, Myrtle E. Long, was secretary of the Iowa State Board of Chiropractic Examiners from 1924 to 1934, and, at the request of appellant George M. Lindsay, she issued a fictitious chiropractic license to appellant George M. Lindsay Jr. for the sum of $250.

Through appellant George M. Lindsay, appellant Debeh secured a fictitious high school diploma, a fictitious medical diploma from the American Medical University, a fictitious certificate of the Arkansas Eclectic Medical Society and a fictitious medical license from the Eclectic State Medical Board of Arkansas, all for the sum of $2,500. Large sums of money were paid in most instances for the spurious diplomas, certificates and licenses. Holders of some of the false diplomas and licenses testified that after receiving them they practiced medicine or chiropractic in various states. Debeh practiced in Arkansas, Pennsylvania, Ohio and West Virginia.

The appellants contended that the evidence did not justify their conviction. But, said the court, there was substantial proof of every element of the crime such as to warrant the jury in finding the appellants guilty. Appellants Date R. Alexander, George M. Lindsay and George M. Lindsay Jr., the court said, were the originators of the fraud. The scheme had for its direct object the defrauding of the public. The issuers of the fraudulent instruments acted through and in conjunction with the practitioners to represent to the public that the latter were duly qualified and legally authorized to practice. The interest of the originators of the scheme did not end when they delivered the diplomas and licenses. This is evidenced by the fact that when their false licensees got into trouble with the authorities they tried to aid and assist them to carry on the deception and gave advice in connection with their attempt to continue practice in certain states.

The evidence showed that Debeh knew nothing about the scheme in its inception. He was one of the persons to whom the bogus documents were issued and not one of the persons who issued them. He however knowingly participated in the scheme as evidenced by a signed statement given to a post office inspector in 1935. He declared that in February 1933 he

had purchased from Lindsay a high school diploma, medical school diploma, certificate of internship and a license to practice medicine in Arkansas for the sum of $2,500. He then went to Little Rock, Ark., and opened an office. Thus, the court said, the evidence clearly supported a finding that during 1933 and 1934 Debeh was working with the other appellants in furtherance of the scheme alleged in the indictment. The fact that he came in long after the plan had had its beginnings or that he did not take part in carrying out each phase of it did not absolve him of complicity.

After reviewing the record at length, the circuit court of appeals could find no error in it. The judgments of conviction were affirmed.—*Alexander v. United States, 95 F. (2d) 873.*

Malpractice: Amputation of Forearm Attributed to Negligent Treatment of Cut on Finger.—The plaintiff sued the defendant, a physician, for malpractice, alleging that by reason of the defendant's negligent treatment of a finger injury the amputation of his forearm became necessary. The trial court gave judgment for the defendant and the plaintiff appealed to the Supreme Court of Michigan.

The plaintiff cut the little finger and palm of his left hand with a meat saw. About two and one-half hours later he consulted the defendant, who washed the cut with Dakin's solution (dilute solution of sodium hypochlorite) and applied a disinfectant powder. Two stitches were taken in the cut and the wound was bandaged. The defendant testified that he placed a pad underneath the hand and then wound 3 or 4 feet of gauze around it to form what he called a figure-of-eight bandage. He testified that the bandage extended to the wrist and bound all four fingers of the hand together, leaving only the thumb free. The plaintiff and two other witnesses, on the other hand, testified that only the wounded finger had been bandaged and that it was not supported by the other fingers. The plaintiff claimed that he was given no advice as to the care of the hand but was merely told to return for further treatment, which he did. The defendant admitted that he did not tell the plaintiff that the hand should be kept quiet and should not be used. The plaintiff was able to, and did, use the injured hand in driving his car and attending to the work around his farm.

The plaintiff visited the defendant's office several times during the two weeks immediately following the accident. When the wound failed to show signs of healing, the defendant advised the plaintiff to bathe the hand in hot water every two hours, but the plaintiff testified that he did this only several times a day. The hand steadily grew worse, and the defendant claimed that on several occasions he told the plaintiff that there was some infection in the wound and that he should go to a hospital but that the plaintiff stated he could not afford to do so. The plaintiff and his wife testified that at no time did the defendant tell the plaintiff to go to a hospital but that he went of his own accord after the defendant had admitted that the hand might be infected. At the hospital a surgeon first removed two joints of the little finger and thereafter, when the hand and arm became steadily worse, the forearm was amputated.

On appeal, the plaintiff's main claim of error was that the verdict was contrary to the weight of the evidence. Four physicians testified that the treatment given the plaintiff was proper and in accordance with the established practice in the community and like communities. One physician testified to the contrary, and another did not entirely exculpate the defendant from blame. There was evidence that one physician who testified in the plaintiff's favor was related to one of his attorneys. All the physicians agreed that proper treatment required immobilization of the plaintiff's hand and two testified that the failure of the defendant to advise the plaintiff to keep his hand quiet and not use it for work was improper practice. However, the court said, there was testimony to the effect that the defendant might properly have assumed that the bandage which he claimed he applied and the pain which would accompany movement would be sufficient to immobilize the hand without specific advice to the patient. The verdict, in the opinion of the court, was not against the great weight of the testimony.

The judgment for the defendant physician was therefore affirmed.—*Moon v. Quick (Mich.), 279 N. W. 909.*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Montgomery, April 18-20. Dr. D. L. Cannon, 519 Dexter Ave., Montgomery, Secretary.
American Association of Anatomists, Boston, Apr. 6-8. Dr. E. R. Clark, University of Pennsylvania School of Medicine, Philadelphia, Secretary.
American Association of Pathologists and Bacteriologists, Richmond, Va., Apr. 6-7. Dr. Howard T. Karsner, 2085 Adelbert Rd., Cleveland, Secretary.
American College of Physicians, New Orleans, March 27-31. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.
American Pediatric Society, Sky Top, Pa., Apr. 27-29. Dr. Hugh McCulloch, 325 North Euclid Ave., St. Louis, Secretary.
American Physiological Society, Toronto, Canada, Apr. 26-29. Dr. A. C. Ivy, 303 East Chicago Ave., Chicago, Secretary.
American Society for Pharmacology and Experimental Therapeutics, Toronto, Canada, Apr. 26-29. Dr. G. Philip Grabfield, 319 Longwood Ave., Boston, Secretary.
American Society of Anesthetists, New York, Apr. 14. Dr. Paul M. Wood, 131 Riverside Drive, New York, Secretary.
American Society of Biological Chemists, Toronto, Canada, Apr. 26-29. Dr. C. G. King, Univ. of Pittsburgh, Dept. of Chemistry, Pittsburgh, Secretary.
Arizona State Medical Association, Phoenix, Apr. 13-15. Dr. D. F. Harbridge, 15 East Monroe St., Phoenix, Secretary.
Federation of American Societies for Experimental Biology, Toronto, Canada, Apr. 26-29. Dr. D. R. Hooker, 19 West Chase St., Baltimore, Secretary.
Georgia, Medical Association of, Atlanta, Apr. 25-28. Dr. Edgar D. Shanks, 478 Peachtree St. N. E., Atlanta, Secretary.
Iowa State Medical Society, Des Moines, Apr. 25-27. Dr. Robert L. Parker, 3510 Sixth Ave., Des Moines, Secretary.
Louisiana State Medical Society, Alexandria, Apr. 24-26. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans, Secretary.
Maryland, Medical and Chirurgical Faculty of, Baltimore, Apr. 25-26. Dr. Walter Dent Wise, 1211 Cathedral St., Baltimore, Secretary.
Missouri State Medical Association, Excelsior Springs, Apr. 10-12. Dr. E. J. Goodwin, 634 North Grand Blvd., St. Louis, Secretary.
New York, Medical Society of the State of, Syracuse, April 24-27. Dr. Peter Irving, 2 East 103d St., New York, Secretary.
Pacific Coast Surgical Association, San Francisco, Oakland, Del Monte, March 28-31. Dr. H. Glenn Bell, University of California Hospital, San Francisco, Secretary.
South Dakota State Medical Association, Aberdeen, Apr. 24-26. Dr. Clarence E. Sherwood, Madison, Secretary.
Southeastern Surgical Congress, Atlanta, Ga., Mar. 6-8. Dr. B. T. Beasley, 701 Hurt Bldg., Atlanta, Ga., Secretary.
Tennessee State Medical Association, Jackson, Apr. 11-13. Dr. H. H. Shoulders, 706 Church St., Nashville, Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Eleventh Annual Meeting, Held in Chicago, Nov. 4 and 5, 1938

The President, DR. WILLIAM H. BUNN, Youngstown, Ohio, in the Chair

Trichinosis in the Chicago Area

MARION HOOD, PH.D., and S. W. OLSEN, B.A., Chicago: Numerous publications indicate that the incidence of trichinosis in the United States is approximately 14 per cent. As no report had been made from the Chicago area a series of 428 cases were studied. The material was obtained from unselected autopsies performed at several Chicago hospitals. Portions of the diaphragm were digested in artificial gastric juice and sedimented. This material was then examined. When approximately 100 Gm. of tissue was used, 16 per cent of the specimens were found infected with Trichina. The results of this work are in accord with those of surveys from other localities. They show that trichinosis is an important problem in the Chicago area.

An Acoustic Study of Stethoscope Behavior

DRS. FRANKLIN D. JOHNSTON and EDWARD M. KLINE, Ann Arbor, Mich.: A cadaver with a telephone receiver placed inside the heart was used as an acoustic model to obtain quantitative data regarding the sound transmitting properties of different stethoscopes. The necessary apparatus was arranged so that when the end pieces of different units were placed at the same point on the intact wall of the chest the response over a wide range of frequency was easily obtained. Tests of different end pieces and tubings indicated that: 1. The shallow chamber bell is superior to other bells, especially for high pitched sounds. 2. A soft rubber nipple placed over the end of a bell improves its performance. 3. The diaphragm on a Bowles unit acts to filter out sounds of low frequency

but it must be stiff to be efficient in this respect. 4. The large Bowles units without the diaphragm are good receptors for sounds of all frequencies and they are further improved when a rubber sheath is placed over the aperture. 5. Although changes in the length, the diameter of the hole and the nature of the rubber in different tubes cause some alterations in the response of a given end piece due to phenomena of absorption and resonance, these differences are relatively small.

DISCUSSION

DR. M. A. BLANKENHORN, Cincinnati: I should like to ask the authors if they can explain why the performance is better with a rubber-covered stethoscope bell and if they have studied or plan to study another important function of stethoscopes besides the transmission of sounds, namely that of excluding other sounds and noises which are so easily excluded from the laboratory but are never excluded from the places where one works. I should like to ask also if they have studied or plan to study the effects of varying pressure of the bell against the wall of the chest. These are all important variables in the hands of the clinician; they are not so important in the laboratory.

DR. FRANKLIN D. JOHNSTON, Ann Arbor, Mich.: When the physician obtains information by the use of the stethoscope a twofold process is involved. First, the stethoscope brings sound energy to the ears and he hears certain things. Second, by experience and training these sounds are separated and interpreted so that rational conclusions are possible. This last process is not measurable, but it is of tremendous importance. Nevertheless, an objective study of the behavior of the stethoscope is valuable so that the beginner, particularly, will not be unnecessarily handicapped by the use of an inferior instrument. In answer to Dr. Blankenhorn's question about how the rubber nipple placed over a bell improves its performance, I really do not know. At first we thought the improvement noted with the nipple was due to a more perfect air-tight seal between the bell and the wall of the chest but this is not the case. When the nipple is used the effective area of contact with the wall of the chest is slightly increased, and this may be a factor. We did no work relating to extraneous sounds, although at many times during the course of the work vibrations coming through the air and especially through the building proved troublesome. I think the only way that extraneous sounds can be dealt with by the physician is through the ability gained, by experience, in disregarding them. The tissues of the cadaver were harder than those in the usual living chest, so that increasing the pressure of the shallow chamber units was not likely to obliterate the terminal air space, as may occur with an inexperienced student of auscultation. This is an important cause for error and should be pointed out to the beginning student. We have no data relating to this matter.

Neosynephrin in Spinal Anesthesia

DRS. ROBBIE BRUNNER and GEZA DE TAKATS, Chicago: The hypotension produced by spinal anesthesia was successfully controlled by the intramuscular injection of neosynephrin hydrochloride in 163 cases. For control, 100 cases were selected in which ephedrine sulfate was used for the same purpose. Aside from the stabilizing effect of neosynephrin on blood pressure, the tachycardia and restlessness produced by ephedrine were absent; on the contrary, bradycardia was produced by neosynephrin, the mechanism of which is analyzed. The drug used with certain precautions and controlled dosage removes one of the great objections to spinal anesthesia, namely the severe fall in blood pressure during and shortly after operation.

DISCUSSION

DR. K. K. CHEN, Indianapolis: There is no question that neosynephrin can be used for the control of the fall in blood pressure in spinal anesthesia. When one talks about the ephedrine group, one should think also of the action on the central nervous system. Formerly physicians emphasized the effect only on the blood pressure, but now it is evident that the action of this group on the central nervous system must be taken into consideration. Freedom from nervous symptoms is an advantage of neosynephrin over ephedrine. However, certain points should be raised and kept in mind. First, there is the question of toxicity. In our laboratory we found that when intravenously injected in mice neosynephrin is 135 times as toxic as ephedrine. The authors use a 10 per cent solution; 0.5 cc. would be 50 mg. and 1 cc. would be 100 mg. In other words, they are employing a dose equivalent to that of ephedrine for spinal anesthesia. Second, the action of neosynephrin is brief, while ephedrine has a much more prolonged effect. Before the use of ephedrine, epinephrine and later tyramine were tried for the maintenance of blood pressure. I should classify neosynephrin as similar to tyramine. The tachycardia under ephedrine depends on the state of the vagus nerve. If atropine is injected first, tachycardia follows the use of ephedrine. On the other hand, if no atropine is administered, either animals or men usually respond by a slowing of the pulse rate. I am certainly much interested in the uniform occurrence of tachycardia with ephedrine therapy.

DR. GEZA DE TAKATS, Chicago: With the use of this drug we have a safeguard against a fall of blood pressure. This has given us a certain degree of confidence, as we have not seen a single instance of lack of response. The blood pressure does not always rise, but at least there is no fall. We give a small dose at the induction of spinal anesthesia and usually ask the anesthetist to inject the second dose of neosynephrin at the time we note the fall. The question of bradycardia was of some interest to us, because most of the patients were elderly and some of them had bradycardia before the operation. Clinically we have not observed any untoward symptoms. In one case a shifting pacemaker developed. When this was observed it was readily abolished with atropine. As regards Dr. Chen's question, I should say that the average duration of the pressor effect of neosynephrin is about thirty minutes. As far as ephedrine is concerned, most of the patients with spinal anesthesia had either no atropine or only $\frac{1}{150}$ grain (0.4 mg.) subcutaneously. We have not noticed any toxic effect with neosynephrin. From 0.5 to 1 cc. of a 1 per cent solution is used. We have used ephedrine for many years with spinal anesthesia. Our only objection to the drug is that in a certain group of patients ephedrine produces restlessness, so that it may be necessary to put them to sleep for no other reason.

Pathogenesis of Hemorrhage in Artificially Induced Fever

DRS. SLOAN J. WILSON and CHARLES A. DOAN, Columbus, Ohio: Petechial hemorrhages have been one of the most constant pathologic observations reported following artificially induced fever. Necropsy on experimental animals and human subjects following lethal fever has revealed extensive hemorrhages and hepatic damage. The mechanism has been attributed to anoxia. In the present survey the influence of fever on the circulating blood platelets, prothrombin and fibrinogen have been studied in experimental animals and in the human subject as possibly important additional contributing factors. Total platelet counts, qualitative and quantitative studies of megakaryocytes in serial sternal marrow punctures, quantitative determinations of prothrombin and fibrinogen and histologic studies of the liver have been made. The hemorrhagic diathesis has been found to be directly proportional to the degree of damage occurring in one or both of these essential factors in the coagulation mechanism.

DISCUSSION

DR. HOWARD L. ALT, Chicago: At present I have under my care a girl aged 7 years who has had artificial fever induced nine times since December 1937 for the treatment of bronchial asthma. The last treatment was given three weeks ago. Ten days ago she began to have ecchymoses, and at the present time she has all the signs of thrombopenic purpura. The platelet count is 20,000 per cubic millimeter. In view of the report of Drs. Wilson and Doan, it seems possible that there is a relation between the artificially induced fever and the purpura in this case.

DR. LEE FOSHAY, Cincinnati: Artificial fever therapy has been used and is being recommended for the treatment of

acute and chronic brucellosis. In this infection the brunt of damage to tissue is often borne by the liver, as evidenced by bilirubinemia, urobilinuria, increased prothrombin time, imperfect retractability of blood clots, subserous hemorrhages, occasionally large retroserosal extravasations of blood and often an enlarged and tender liver. I do not wish to be understood as advising against fever therapy in this disease, but I suggest that the facts presented by Wilson and Doan warrant extremely careful selection and preparation of patients with brucellosis before fever therapy is attempted.

DR. E. P. K. FENGER, Rochester, Minn.: I wonder whether studies have been made of giving oxygen with fever therapy. There is known to be a consumption of about seven degrees of oxygen with fever. If studies were made with a view of giving oxygen with fever therapy it might head off these deleterious effects.

DR. SLOAN J. WILSON, Columbus, Ohio: Oxygen has been given intranasally during fever therapy to prevent anoxia. Hartman prevented a decrease of oxygen in the venous and arterial blood of experimental animals by the intranasal administration of oxygen. He was the first to suggest that oxygen be given to patients during fever therapy. He also stated that the efficacy of the barbiturates is decreased when oxygen is given.

Production of Hepatic Disease by Dietary Deficiency and Its Effect on the Anti-Pernicious Anemia Principle

DR. FRANK H. BETHELL, Ann Arbor, Mich.: Extensive lipoidosis of the liver was produced in pregnant and in nonpregnant rats by diets possessing the relatively low protein contents of 8 per cent and 3 per cent respectively. Associated with hepatic damage there were macrocytic anemia and a megaloblastic reaction of the bone marrow. These changes could not be prevented by oral or parenteral administration of liver extract or by a high intake of yeast. Extracts made from the livers of experimental animals were administered parenterally to five patients with pernicious anemia in relapse. By means of the double reticulocyte response, normal rat liver extract being used as a control, a deficiency of the anti-pernicious anemia principle was demonstrated in the livers of rats made anemic by protein deficient diets.

DISCUSSION

DR. C. J. WATSON, Minneapolis: Was the reticulocyte count spontaneously elevated in rat anemia while the hemoglobin and the red blood cell level were falling?

DR. O. O. MEYER, Madison, Wis.: I should like to ask whether the livers of the rats on deficient diets were larger than normal, and whether the speaker thought the deficiency in diet was responsible. Also was the extract made from a certain number of grams of liver or was it made by comparing rat for rat? It is possible that the difference in results may be due merely to the factor of dilution.

DR. FRANK H. BETHELL, Ann Arbor, Mich.: In answer to Dr. Watson's question, the reticulocyte counts of the rats with macrocytic anemia were elevated. In the rat the number of the reticulocytes fluctuates widely and is increased in almost every form of anemia. With regard to Dr. Meyer's question, the livers of the anemic rats were slightly enlarged in proportion to the size of the rats. The doses of extracts were based on the grams of liver from which they were derived, not on the weights of the individual rats. The latter method would not be suitable because of the general undernutrition of rats on low protein diets. The weight of the liver of rats on low protein diets was slightly less than that of animals on high protein diets, owing in part, at least, to the lower specific gravity of fat.

Monocytic Leukemia of the Schilling and the Naegeli Type

DRS. CHARLES H. WATKINS and BYRON E. HALL, Rochester, Minn.: Two types of monocytic leukemia are now generally recognized—the so-called Naegeli type, which many authorities regard as a variant of myelogenous leukemia with a predominance of monocytes, and the Schilling type, which presumably is a variant form of leukemic reticulo-endotheliosis in which the monocytes are derived directly from reticular cells. In the past ten years we have observed twenty cases of the Naegeli type and four cases of the Schilling type. These two groups of cases are compared with respect to the clinical manifestations (age, sex, presenting symptoms, duration of illness and response to x-ray or radium therapy when either was given) as well as with regard to the hematologic and histologic pictures.

DISCUSSION

DR. RAPHAEL ISAACS, Ann Arbor, Mich: In myelogenous leukemia immature monocytes may be pushed out of the bone marrow (Naegeli type of "monocytic leukemia") and in monocytic leukemia immature polymorphonuclear cell stages may be forced into the peripheral circulation (Schilling type of monocytic leukemia). Three clinical features help to distinguish monocytic leukemia from the myelogenous type. In the first the liver and spleen are enlarged to about the same linear measurement, whereas in the second the spleen eventually becomes disproportionately elongated. Oral lesions (ulcerative) are more frequent in true monocytic leukemia than in the myelogenous type. True monocytic leukemia responds poorly to roentgen therapy but does respond to arsenical medication. Our present view is that "myelogenous" leukemia which responds to arsenic is in reality monocytic. It is easy to tell the monoblast from the myeloblast or lymphoblast, as the true monoblast is the only one in which granules (red staining) appear in the cytoplasm.

DR. BYRON E. HALL, Rochester, Minn.: There are many different views concerning the origin and developmental potencies of the mononuclear elements in the blood and blood-forming organs. This is particularly true of the monocyte. However, we feel that the separation of monocytic leukemia into two groups is justified not only on the basis of the difference in the blood picture and the type of stem cell from which the monocyte is derived but because of the pathologic differences of the hemopoietic organs in each condition. It was our impression when we began this study that infiltration of the gums was more common in acute monocytic leukemia than in other forms of acute leukemia. As Dr. Isaacs stated, this feature has been emphasized by many clinicians. We were therefore somewhat surprised to find that in our series lesions of the gums were no more frequent in monocytic leukemia than in myelogenous and other types of leukemia. As far as a comparison of the size of organs is concerned, in the Schilling group the liver was not palpable in any case, but enlargement of the spleen was demonstrable in all four cases and slight enlargement of the lymph nodes was noted in half of them. In the Naegeli group definite but in most cases slight enlargement of the lymph nodes was found in all but two cases; enlargement of the spleen was demonstrable in fifteen, and enlargement of the liver was noted in thirteen of the twenty cases. Dr. Isaacs stated that azure granules are observed only in monoblasts. We have seen azure granulations in the cytoplasm of stem cells in the Naegeli type of monocytic leukemia (monoblasts of many authors). They are common in genuine myeloblasts, as Naegeli, Pappenheim and others demonstrated many years ago, and frequently are seen in these cells in cases of myelogenous leukemia. In myelogenous leukemia one or several cellular lineages may be affected. For example, there have been many reports in the literature of eosinophilic leukemia. There are also cases on record of neutrophilic, basophilic and megakaryocytic leukemia. In each instance a single type of cell is involved primarily. In many of these cases, however, there has been a picture characteristic of chronic myelogenous leukemia during later stages of the disease. In the usual case of chronic myelogenous leukemia the majority if not all types of myeloid elements are involved in the leukemic process (panmyelosis). It is our opinion that the eosinophilic, basophilic and megakaryocytic types of leukemia are variant forms of myelogenous leukemia. The monocyte likewise may be primarily affected, being derived from the myeloblast. We have attempted to show that cases in which this occurs differ hematologically and pathologically from cases of leukemic reticulo-endotheliosis and that they should be classified as instances of a form of myelogenous leukemia.

Bone Marrow in the Active Phase of Essential Thrombopenic Purpura

DR. LOUIS R. LIMARZI and EMIL M. SCHLEICHER, M.S., Chicago: Although essential thrombopenic purpura has been extensively studied, little attention has been paid to the bone marrow. In our studies of this disease during the active phase (four cases) the bone marrow showed a megakaryocytic hyperplasia with the presence of many young forms (promegakaryocytes). At this time the peripheral blood shows a reduction in number and an abnormality in size of the platelets. These characteristics of the bone marrow persist through remissions induced by blood transfusion, even though the peripheral blood has shown a moderate increase in the number of platelets. After splenectomy the bone marrow approaches normal with an increase in the platelets in the peripheral blood and a cessation of bleeding. In one patient whose episodes of bleeding were reduced but not abolished after splenectomy the bone marrow still shows megakaryocytic hyperplasia with immature forms. Studies of bone marrow make possible an accurate differentiation of essential thrombopenic purpura from other inaccurately diagnosed hemorrhagic states (aleukemic myelosis, aplastic anemia and toxic purpura).

DISCUSSION

DR. FRANK H. BETHELL, Ann Arbor, Mich.: I have been performing sternal aspiration before deciding on splenectomy in cases of thrombopenic purpura. I agree with the authors that the procedure is of diagnostic value but I do not think that, for practical purposes, it is necessary to carry out such an involved technic as they have described. I aspirate a small amount of material from the sternum and make cover slip films at the bedside without the use of an anticoagulant. These reveal the characteristic increase in megakaryocytes in patients suitable for splenectomy.

DR. LOUIS R. LIMARZI, Chicago: In our first studies of bone marrow we followed the usual procedure in obtaining marrow. The advantage of the method we described is that sinusoidal blood and fat are separated from the bone marrow cells. In other words, one obtains a concentration of marrow cells. It also offers a method of studying gross quantitative changes that take place in diseases like pernicious anemia or microcytic hypochromic anemia before and after the institution of therapy. This method of studying bone marrow has been followed in 600 patients as young as 6 weeks and as old as 80 years.

A Specific Cell in the Peripheral Blood, Characteristic of Liver Disease

DR. RAPHAEL ISAACS, Ann Arbor, Mich.: Characteristic of hepatic disease (cirrhosis, chronic passive congestion, hepatitis, secondary hepatic disturbance in obstructive jaundice and cholecystitis, leukemia) is the appearance in the blood stream of a specific cell which may constitute from 1 to 15 per cent of the leukocytes. The cells have an irregular wavy margin, with pseudopodia-like projections in the older forms. The average size varies from 15 by 13 to 18 by 18 microns, with an oval nucleus averaging 12 by 9 microns. The cytoplasm stains a sky blue and has a foamy structure like that of a monocyte, but the minute red-staining granules of the latter are absent. A few large red-staining granules may be present. The tips of the pseudopods are hyaline. The chromatin in the nucleus is coarse with a heavy reticulum but is frequently so dense that but little detail of structure can be seen. There is no discrete nuclear membrane. There is no perinuclear clear zone, as in lymphocytes. With brilliant cresyl blue applied while the cells are wet, and counterstaining with Wright's stain when dry, the cresyl blue granulation is in heavy masses near the nucleus and in finer particles near the periphery. Many of the cells with this stain show a clear pink-staining hyaline ectoplasm. The cells appear in the peripheral circulation in experimental liver poisoning in animals.

The Clotting Time of Hemophilic Blood

DR. ARMAND J. QUICK, Milwaukee: If thromboplastin is added hemophilic blood will coagulate as rapidly as normal blood, which indicates that a deficiency of thromboplastin is the probable cause of the defective clotting. Furthermore, when oxalated hemophilic blood is centrifuged at a high speed the plasma on recalcification will coagulate much more slowly than if the plasma is obtained by a low rate of centrifugation. The coagulation of plasma from normal blood is only slightly influenced by the speed of centrifugation. This suggests that the platelets in hemophilia are more resistant to lysis and are removed by rapid centrifuging, thus leaving the plasma poor in thromboplastin. When oxalated hemophilic plasma is allowed to stand, its coagulation time when recalcified will become progressively shorter and will approach normal. These observations make it seem probable that the cause of the prolonged clotting time in hemophilia is the slow liberation of thromboplastin from platelets rather than the absence of any factor essential for coagulation.

DISCUSSION

DR. CARROLL F. BIRCH, Chicago: As Dr. Quick says, the important question is Why do the platelets not break up? One group of authors believes that the platelets have an actual increase in mechanical resistance, while another group holds that the platelets are normal although placed in an abnormal environment, hemophiliac plasma. The latter group bases its evidence on the fact that hemophiliac platelets behave normally when placed in normal plasma; they agglutinate and rupture within the average time.

Leukothrombopenia with Increased Capillary Permeability

DRS. FREDERICK W. MADISON and THEODORE L. SQUIER, Milwaukee: We have observed three adults with severe leukopenia, thrombopenia and strongly positive Rumpel-Leeds phenomena. The presenting complaints were extensive suppurative lesions in two and pathologic bleeding in one. In each, recovery from clinical symptoms occurred, but the two with pyogenic lesions thus far have made only partial hematologic recovery. Drug origin was ruled out in each. The erythrocyte count was not significantly involved in any case and responded to ordinary therapeutic procedures. In each instance the leukocyte and thrombocyte counts and the abnormal capillary permeability failed to respond to all medication except the use of epinephrine in one. We believe the leukothrombopenia present in these three patients is a definite clinical syndrome representing another manifestation of the selective, reversible inhibition of bone marrow seen in agranulocytic angina and in some cases of thrombopenic purpura. One of the three patients was found sensitive to milk and made prompt symptomatic and hematologic recovery under allergic control alone. In our opinion it is important to differentiate leukothrombopenia from typical agranulocytic angina and from leukopenic leukemia because of the difference in the clinical course, prognosis and therapeutic management.

Oral and Intramuscular Administration of Vitamin K in Hemorrhagic Diathesis of Obstructive Jaundice

DRS. HUGH R. BUTT and ALBERT M. SNELL and ARNOLD E. OSTERBERG, PH.D., Rochester, Minn.: The effect of concentrates of vitamin K prepared from various sources and administered orally and intramuscularly has been studied with reference to the qualitative and quantitative level of prothrombin during the preoperative and postoperative course in cases of various types of obstructive jaundice. A rough inverse relation between prothrombin coagulation time and quantitative prothrombin levels can be demonstrated. The intramuscular administration of the vitamin, while effective in K-avitaminous chicks, is considerably less useful in the human subject than is the oral administration of the preparation. A fall in quantitative prothrombin has been demonstrated postoperatively in a number of cases, a fact which emphasizes the necessity for careful observation.

DISCUSSION

DR. EMORY D. WARNER, Iowa City: I should like to ask the authors first what, in their experience, is the level for prothrombin below which the patient is likely to bleed, and second, what, if any, correlation they have been able to work out between the extent of the decrease in prothrombin and the

duration and the intensity of the jaundice. I have had three cases in which the prothrombin was at a low level and in which I got no prothrombin response by feeding vitamin K concentrate. The patients had advanced hepatic damage in the form of biliary cirrhosis. I felt that the hepatic damage accounted for the failure to respond to vitamin K therapy. It has been shown that hepatic damage will cause lowering of the prothrombin content of the plasma—almost to the vanishing point if the damage is extreme, as in chloroform poisoning in dogs. It is to be expected that in patients with extreme hepatic damage a response to vitamin K therapy cannot be obtained because the injured liver is incapable of producing prothrombin.

DR. E. L. TUOHY, Duluth, Minn.: Does the test for prothrombin furnish some index of hepatic capacity or function? Through the courtesy of Drs. Butt and Snell I had the opportunity to test out this material, with extremely favorable results, in a patient with carcinoma of the head of the pancreas, with painless, rapidly developing jaundice and a tendency to bleed. I gave it both preoperatively and postoperatively, and the response was exactly as the authors have shown. I should like to ask further if with this method of controlling jaundice there is any further need of attempting to rely to any degree on the administration of calcium, which formerly seems to have given the surgeons considerable comfort.

DR. M. A. BLANKENHORN, Cincinnati: Is the plan of treatment the same when the bile is returned to the intestine at operation by anastomosis of the gallbladder as when the bile continues to be excluded from the intestine?

DR. HEINRICH NECHELES, Chicago: Did these jaundiced patients with normal prothrombin time who did not receive any treatment with bile salts, blood transfusions or vitamin K bleed nevertheless?

DR. RUSSELL M. WILDER, Rochester, Minn.: Vitamin K occurs in many foods, so deficiency of it in diets is extraordinary. I should like to ask the authors to add a word about the effect of giving bile alone without vitamin K in these cases with diminished lengthening of the prothrombin time.

DR. ARMAND J. QUICK, Milwaukee: This report indicates that clinical study of the problem has gone much further and has been much more successful than the laboratory study. The determination of prothrombin is at best a difficult matter. I fail to understand why there should be a difference in the results of the two methods used, the prothrombin time and the method developed by Dr. Smith and his co-workers. It means that there is still a great deal to be known about prothrombin. I might say that many of these jaundiced patients have slightly antithrombic plasma—in other words, it inhibits the action of thrombin, which might account for a more prolonged prothrombin time than can be accounted for by the actual decrease in prothrombin. If the plasma is highly concentrated, coagulation will be delayed. I just want to point out that the problem is still open as far as experimental work is concerned.

DR. HUGH R. BUTT, Rochester, Minn.: Warner, Brinkhous and Smith of the University of Iowa have reported that, in dogs with a quantitative level of prothrombin below 20 per cent, bleeding usually occurs. In man, however, the critical level of prothrombin at which bleeding occurs seems to be much higher. We have seen bleeding occur in man with a quantitative level of prothrombin as high as 40 or 50 per cent. I know of no theoretical explanation for this phenomenon, but Dr. Smith also feels that perhaps the critical level of prothrombin at which bleeding occurs for some reason is higher than that of dogs. We have noted some similarity between the elevation of the bilirubin content of the serum and the elevation of the prothrombin clotting time. It is well known that the hemorrhagic diathesis in patients with jaundice occurs most often when no bile is able to enter the intestinal tract. Certain groups of patients seem to bleed more frequently than others, and the frequent tendency to bleed is likely to occur from the following causes in order: (1) anatomic obstruction, such as occurs in carcinoma of the head of the pancreas or biliary ducts, (2) stricture of the biliary ducts, (3) complete external biliary fistula, (4) stone in the biliary duct and (5) diffuse hepatitis. In such cases we have often noted that as the bilirubin content rises the level of prothrombin in the circulating blood decreases. I was interested to hear Dr. Warner say that he had observed three patients who did not respond to the administration of vitamin K and bile salts. No doubt as more cases are observed all physicians will have a similar experience. The condition perhaps represents an irreversible reaction such as can be observed in many other diseases due to vitamin deficiency.

In reply to Dr. Tuohy, the use of the level of prothrombin as an indication of hepatic function has been fairly well established by the work of Warner, Brinkhous and Smith. By injuring the liver of dogs with chloroform, they have shown that the level of prothrombin is decreased. From their studies they have suggested that the liver perhaps plays a major role in either the fabrication or the activation of the substance called prothrombin. Calcium chloride formerly was believed, and still is by some physicians, to be useful in the treatment of the hemorrhagic diathesis in patients with jaundice, and I believe that it has been well demonstrated by Walters and others to be of distinct benefit. However, the results of experimental research on this problem do not coincide with those of clinical experience. It has been rather definitely shown that the amount of calcium in any of its forms is not appreciably altered in patients with jaundice. Nevertheless, in spite of these theoretical data I do not see any harm in giving calcium, and certainly, since the problem of bleeding is still far from settled, it would seem that an excess of any material necessary for blood clotting might be of some benefit.

Dr. Blankenhorn has asked about the importance of reestablishing the flow of bile into the intestinal tract and Dr. Wilder wishes a more detailed explanation of the value of bile salts. The use of bile salts is based on the fact that in hepatic injury from any cause, and particularly when there is obstruction to the outflow of bile, the quantity and quality of bile salts entering the intestinal tract are poor. It has been well established that the presence of bile salts is necessary for proper absorption of fat-soluble materials. It is assumed that the substance called vitamin K comprises one or more fat-soluble substances, and for this reason bile salts are given to aid in better utilization of this material. Obviously, the first thing of importance is to reestablish the normal flow of bile into the intestinal tract. However, even after this is accomplished, the amount and quality of bile salts entering the intestine is poor. For this reason, we feel that the supplementary use of animal bile salts is important. It is true that if a patient is eating a diet which contains adequate amounts of vitamin K, provided he has only a mild degree of prothrombin deficiency, bile salts alone seem to be sufficient to maintain a proper level of prothrombin. However, if the prothrombin level is greatly decreased, bile salts alone have not proved as effective as vitamin K and bile salts administered together. We have not seen bleeding in patients who had a normal prothrombin clotting time. No doubt, as I have mentioned before, it can occur, since one cannot accurately predict from a single determination of prothrombin clotting time just what is the quantitative level of prothrombin in the circulating blood. As I have just demonstrated, in the patient with a stricture of the common duct the prothrombin clotting time was thirty seconds, while the quantitative level of prothrombin was 38 per cent of normal.

I agree with Dr. Quick that it is difficult to explain just why the quantitative measurement of prothrombin developed by Warner, Brinkhous and Smith does not check more closely than it does with the measurement of prothrombin clotting time developed by Dr. Quick. It seems to me that this discrepancy probably can be explained by the facts first that both methods are indirect measurements of the substance called prothrombin and second that little is known about the substance designated as prothrombin. It is true that it is thought to be a protein, but little is known of its physical or chemical nature, and until these facts are known the question which Dr. Quick has raised must remain unanswered. We do feel that the methods of measuring prothrombin developed by the two groups of workers are good. The method developed by Quick seems to be better adapted for use in the average clinical laboratory. However, for detailed research in this problem, the quantitative method developed by Warner, Brinkhous and Smith is invaluable.

(To be continued)

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

197: 1-140 (Jan.) 1939

The "Romantic" Attributes of "Lawlessness" and "Malignancy" in Cancer. H. Oertel, Montreal.—p. 1.

Localization of Cardiac Infarcts in Man: I. Comparison of Anterior-Posterior with Muscle Bundle Modes of Localization. Jane Sands Robb and R. C. Robb, Syracuse, N. Y.—p. 7.

Id.: II. Twenty-Nine New Cases of Muscle Bundle Localization with Postmortem Confirmation. Jane Sands Robb and R. C. Robb, Syracuse, N. Y.—p. 18.

*Treatment of Pneumococcic Pneumonia by Hydroxyethylapocupreine. W. W. G. Maclachlan, J. M. Johnston, M. M. Bracken and G. E. Crum, Pittsburgh.—p. 31.

The Blood Platelet Count in Relation to the Menstrual Cycle in Normal Women. F. J. Pohle, Boston.—p. 40.

*The Present Incidence of Trichinella Spiralis in Man as Determined by a Study of 1,060 Unselected Autopsies in St. Louis Hospitals. T. B. Pote, St. Louis.—p. 47.

*Effect of Induced Hyperpyrexia on the Urea Clearance of Rheumatic Patients. L. E. Farr and J. K. Moen, New York.—p. 53.

Effect of Benzedrine, Benzedrine and Atropine, and Atropine on the Gallbladder. P. G. Schube, A. Myerson and R. Lambert, Boston.—p. 57.

Pathologic Physiology of Pulmonary Cysts and Emphysematous Bullae. N. L. Kaltreider and W. W. Fray, Rochester, N. Y.—p. 62.

Effects of Large Doses of Insulin on Blood Hydration in Man. S. Koppelman, Philadelphia.—p. 78.

Hyperparathyroidism Due to Parathyroid Adenoma, with Death from Parathormone Intoxication. F. M. Hanes, Durham, N. C.—p. 85.

Notes on Chemical Studies of a Gaucher Spleen. Jeanette S. McConnell, J. C. Forbes and F. L. Apperly, Richmond, Va.—p. 90.

Hodgkin's Disease with Massive Collapse and Cavitation of the Lung: Case. B. L. Hardin Jr., Washington, D. C.—p. 92.

Venous Blood Pressure Measurements During Syncope Caused by Hyperirritable Carotid Sinus Reflex. L. J. Robinson, Palmer, Mass.—p. 100.

Pressor Effect of Amphetamine (Benzedrine) on Normal, Hypotensive and Hypertensive Patients. W. W. Dyer, Philadelphia.—p. 103.

Hydroxyethylapocupreine for Pneumonia.—Maclachlan and his collaborators gave hydroxyethylapocupreine dihydrochloride to 149 patients with pneumococcic pneumonia. The substance was taken orally in capsule form, 15 grains (1 Gm.) every three hours day and night for from three to five days. In some cases it produced nausea and occasionally vomiting. However, in only a few cases was it necessary to discontinue the drug for this reason. For intravenous use a monohydrochloride solution is given, each 50 cc. containing 15 grains, and this is injected into the vein every three hours. The intravenous solution is given slowly, in from seven to ten minutes. No patient less than 15 years of age has been treated with this substance. During the last year, of the authors' 149 chemically treated patients pneumococcic empyema developed in two, with surgical drainage and recovery. The mortality figure in pneumococcic pneumonia in adults during the last year has been greatly reduced in those patients who received hydroxyethylapocupreine. A comparison of the mortality figures of the chemically treated cases, which were smaller in number, with the serum-treated cases in Pittsburgh for the same types of pneumonia, during the same period of time, shows almost identical results. Hydroxyethylapocupreine in this series has shown no evidence of disturbing vision.

Incidence of Trichinella Spiralis in Man.—Pote gives the results of examining muscular tissue for trichinella larvae tissue from 1,060 unselected necropsies at Barnes and St. Louis City hospitals. All the subjects were more than 15 years of age and had died during hospitalization from some disease other than trichiniasis. Of these necropsies, on the bodies of individuals never suspected of having trichiniasis during life, 163 (15.37 per cent) showed the presence of trichinella larvae in the muscles. The parasites were apparently dead in 95 per cent of the cases. In two subjects, one 17 and the other 19 years of age, the trichinellae were completely calcified. On the other hand, in some cases the parasites moved vigorously and often continued to show signs of life for from one to six days after the muscle had been removed. The presence of live parasites was also demonstrated by feeding infested muscle to white rats and recovering the larval forms at the end of forty days. By these means viable parasites were shown in 5 per cent of the positive cases. The occupation of the infested subjects was determined but no significant association with any line of work was apparent. In 1,500 hog carcasses examined for trichinella, 0.8 per cent were found to be infested, which gives rise to the question whether man is getting all of his trichinella infestation from pork. It may be concluded that man's infestation comes from pork derived from the small packing plants which are not supervised by meat inspection services. It is to be noted that the infestations that occur sporadically are from pork from the establishments not under federal inspection. The author concludes that Trichinella spiralis infestation of man is not a serious lethal factor in Missouri, since in the 163 instances of infestation it was not held to have contributed to the actual cause of death.

Urea Clearance After Hyperpyrexia in Rheumatic Patients.—Farr and Moen performed urea clearance tests on seven rheumatic patients before, during and after artificially induced hyperpyrexia. Of these seven patients two had rheumatic fever, three had subacute or chronic infectious arthritis, one had gonococcic arthritis and one had dermatomyositis. The average urea clearance during the period when the temperature was rising was 61.7 per cent of normal and during the period when the temperature was at a maximum the clearance averaged 75 per cent of normal. In two instances a severe oliguria resulted from the treatment, and these patients were able to void only after twelve hours. For the entire group the average control clearance was 105 per cent when the patients were afebrile. The data indicate that dehydration should be avoided during fever therapy.

American Journal of Physiology, Baltimore

125: 1-204 (Jan.) 1939. Partial Index

Effect of Zinc on Insulin and Its Mechanism. M. Sahyun, Detroit.—p. 24.

Maintenance of Pregnancy by Progesterone in Rabbits Castrated on the Eleventh Day. W. M. Allen and G. P. Heckel, Rochester, N. Y.—p. 31.

Ease of Body Heat Loss as a Basic Developmental and Functional Factor in Warm Blooded Animals. C. A. Mills and Cordelia Ogle.—p. 36.

Kidney Function in Adrenal Cortical Insufficiency. I. Gersh and A. Grollman, Baltimore.—p. 66.

Effect of Intravenous Injections of Heparin in the Dog. L. B. Jaques, Toronto.—p. 98.

Mechanism of Action of Saliva in Blood Coagulation. A. J. Glazko and D. M. Greenberg, Berkeley, Calif.—p. 108.

Effects of Formalin on Thyroid Stimulating and Gonadotropic Hormones of Cattle Anterior Pituitary Glands. S. J. Hayward, J. H. Pollock and L. Loeb, St. Louis.—p. 113.

Cervical Sympathetic Stimulation and Basal Metabolism. H. B. Friedgood and S. Bevin, Boston.—p. 153.

Electrocardiographic Changes and Concentration of Calcium in Serum Following Intravenous Injection of Calcium Chloride. H. E. Hoff, P. K. Smith and A. W. Winkler, New Haven, Conn.—p. 162.

Manner of Strychnine Action on Nervous System. P. Heinbecker and S. H. Bartley, St. Louis.—p. 172.

*Persistent Diabetes Following Injection of Anterior Pituitary Extract. F. C. Dohan and F. D. W. Lukens, Philadelphia.—p. 188.

Defatiguing Effect of Adrenalin. J. V. Luco, Boston.—p. 196.

Persistent Diabetes After Pituitary Extract.—Dohan and Lukens confirm the work of Young, who has recently described the production in dogs of diabetes, which continued for months after the cessation of intraperitoneal injections of increasingly larger doses of a carefully prepared extract of the anterior pituitary gland, of Campbell and Best, who have had a similar experience, and of Evans, who reported the persistence of diabetes in two dogs after approximately nine months of treatment with a growth hormone preparation. The present report adds metabolic studies to illustrate the character of the diabetes so induced. While the intensity of the diabetes varied, the metabolic behavior of the animals was similar to that of partially depancreatized dogs. Histologic evidence also indicates damage to the islands of Langerhans.

Archives of Ophthalmology, Chicago

21: 1-210 (Jan.) 1939

Correction of Ptosis by Attachment of Strips of Orbicularis Muscle to the Superior Rectus Muscle. J. M. Wheeler, New York.—p. 1.
Role of Nonviolence in Lever Action Intracapsular Extraction of Cataract. K. C. Dutt, Sonpur Raj, India.—p. 8.
New Method for Transplanting Pterygium. E. M. Neher, Salt Lake City.—p. 30.
Some Physiologic and Pharmacologic Reactions of Isolated Iris Muscles. P. Heath and C. W. Geiter, Detroit.—p. 35.
Congenital Cyst of the Vitreous. J. V. Cassady, South Bend, Ind.—p. 45.
*Ocular Manifestations in Brucellosis (Undulant Fever). J. Green, St. Louis.—p. 51.
Malignant Melanoma of the Choroid with Metastases: Report of Case. F. J. Pinkerton, Honolulu, Hawaii.—p. 68.
Higher Visibility in a Roentgenogram Illuminator. C. E. Ferree and G. Rand, Baltimore.—p. 70.
Vascular Obliteration for Various Types of Keratitis: Its Significance Regarding Nutrition of Corneal Epithelium. T. Gundersen, Boston.—p. 76.
Congenital Grouped Pigmentation of the Retina: Report of Case. C. A. Perera, New York.—p. 108.
Retinal Arteriolar Changes as Part of an Induced General Vasospastic Reaction: Effect of Tobacco and Cold. P. L. Cusick and W. E. Herrell, Rochester, Minn.—p. 111.
Herpes Zoster Ophthalmicus: Report of Case. F. L. P. Koch, Rochester, Minn.—p. 118.
Ectopia Lentis: Pathologic and Clinical Study. C. C. Clarke, New Haven, Conn.—p. 124.

Ocular Manifestations in Brucellosis.—Green believes that since ocular manifestations occur in brucellosis more ophthalmologists, when confronted with a case in which the etiology is not determined, should take advantage of the opportunity to determine by laboratory methods the presence or absence of past or present infection with Brucella. Most ocular lesions occurring in the course of brucellosis do not destroy the integrity of the globe. Hence enucleation is not imperative. This fact explains the lack of any pathologic examination of a human eye that has been affected with brucellosis. Evidence is accumulating that some ocular maladies heretofore ascribed to other origins may be caused by brucellosis. The external ocular muscles, the cornea, the uveal tract, the retina and the optic nerve have all proved vulnerable. Almost every physician has been thwarted in his efforts to establish the cause of a chronic uveitis. The ophthalmologist should include in his list of possible etiologic factors a disease that is widespread and one that has been proved capable of affecting almost every tissue of the body (brucellosis).

Archives of Otolaryngology, Chicago

29: 1-198 (Jan.) 1939

Parapharyngeal Hemorrhage: Diagnosis and Treatment. F. W. White and L. Hubert, New York.—p. 1.
Relation of Internal Ear Spaces to Meninges. H. B. Perlman and J. R. Lindsay, Chicago.—p. 12.
Osteomyelitis of Skull Complicating Mastoiditis and Frontal Sinusitis: Report of Two Cases. O. C. Hirst, Philadelphia.—p. 24.
Unusual Form of Nasal Headache. W. G. Mussun, Cleveland.—p. 39.
Thrombosis of the Lateral Sinus: Study of Fifteen Cases, Including Histologic Examination. J. G. Druss, New York.—p. 42.
Incidence of Malignant Tumors of the Head and Neck: Statistical Survey. N. D. Fabricant, Chicago.—p. 65.
Laryngeal Stenosis in Children, with Special Reference to Treatment with Core Molds. E. J. Patterson, Pittsburgh.—p. 71.
Lingual Thyroid. C. Smith, Spokane, Wash.—p. 78.
Otitis Media and Orbital Cellulitis Complicating Scarlet Fever: Preliminary Report on Loss of Hearing from This Disease. H. J. Williams, Philadelphia.—p. 82.
The Larynx in Infancy: Study of Chronic Stridor. C. A. Heatly, Rochester, N. Y.—p. 90.
*Chemoprophylaxis Against Impending Poliomyelitis. Rea E. Ashley, San Francisco.—p. 104.
*Irritation of the Throat from Cigaret Smoke: Study of Hygroscopic Agents. H. C. Ballenger, Chicago.—p. 115.
Galvanic Reaction in Guinea Pigs: I. Normal Galvanic Reaction. A. R. Buchanan and Laura D. Ladd, University, Miss.—p. 124.
Id.: II. Reaction Following Labyrinthectomy. A. R. Buchanan and Laura D. Ladd, University, Miss.—p. 136.
Functional Examination of Hearing. R. Sonnenschein and N. Leshin, Chicago.—p. 164.

Chemoprophylaxis for Poliomyelitis.—According to Ashley, the experimental work of Armstrong, Schultz and their collaborators offered the first definite hope of controlling infantile paralysis by the nasal instillation of chemicals. Up to this time immune serums and vaccines failed to protect monkeys against the inoculation of the virus. Their work paved the way for trials of chemicals in preventing the disease in human beings. Certain chemicals applied to the olfactory tracts of monkeys have rendered the animals resistant to infection with the virus after repeated intranasal instillation. Fifty or sixty chemicals have been tested for this protective property, and while zinc sulfate is not toxic and seems to be the most effective it causes certain irritating and unpleasant symptoms and is not the ideal solution. Anosmia which develops after chemical treatment is probably an evidence of the completeness of the nerve blocking and an indication of the protection. The duration of the anosmia when zinc sulfate is used varies greatly in different persons, but apparently the sense of smell always returns. If this type of treatment is practical, the effectiveness of the protection will depend on the thoroughness of the nerve blocking. Functional tests for the return of the sense of smell should be the guide for further chemical application. While the experience during human epidemics has so far failed to show definite protection, further trials are indicated since previous methods of application have been faulty. If this treatment proves effective in man it will still not be an ideal prophylactic, as the protection afforded is short and as it fails to produce any immunity in the individual to the virus. Nevertheless it is the only method available which promises any hope of actually combating the disease.

Throat Irritation from Cigaret Smoke.—Ballenger did not find, after a careful objective examination of 102 cigaret smokers, any significant difference in the irritation of the mucosa of the nose or throat from smoking cigarets moistened with glycerin, those moistened with diethylene glycol or those with no hygroscopic agent. The subjective symptoms or sensations of irritation, when present, were not marked enough in respect to distribution, character or degree to justify definite conclusions. Lymphoid hyperplasia of the pharynx does not appear to have any relation to the number of cigarets smoked.

Archives of Physical Therapy, Chicago

19: 721-784 (Dec.) 1938

Dosage Measurement in Short Wave Diathermy. E. Mittelmann and D. Kobak, Chicago.—p. 725.
Athermic Short Wave Therapy. P. Liebesny, New York.—p. 736.
Effect of the Elliott Treatment on Nasal Membrane. F. L. Bryant, Minneapolis.—p. 740.
Elliott Therapy in Ophthalmology. M. S. Udelf, Cleveland.—p. 744.
Fever Therapy at High Humidities. W. Finkelstein, New York.—p. 748.
Rehabilitation of the Physically Handicapped. H. H. Kessler, Newark, N. J.—p. 753.
Treatment of Colon Infestation by Irrigation and Hot Instillations. D. de Rivas, Philadelphia.—p. 756.

Arkansas Medical Society Journal, Fort Smith

35: 141-162 (Jan.) 1939

Exploitation of the Medical Profession. J. S. Jenkins, Pine Bluff.—p. 141.
Intra-Ocular Tumors. A. W. Roberts, Texarkana.—p. 145.

Bulletin New York Academy of Medicine, New York

15: 1-60 (Jan.) 1939

Hemophilia. W. H. Howell, Baltimore.—p. 3.
Some Aspects of Intermediary Metabolism of the Steroid Hormones. G. F. Marrian, Toronto.—p. 27.
*Infectious Mononucleosis. J. R. Paul, New Haven, Conn.—p. 43.

Infectious Mononucleosis.—Paul believes that there are few diseases in which one is so fortunate as to have three definite diagnostic aids (clinical picture, blood counts and serologic test) and yet, in spite of them, the disease probably often escapes recognition. Sometimes the clinical symptoms are mild; there seems to be such a thing as "walking infectious mononucleosis" and these and other cases may easily escape recognition if differential blood counts are not done. The classic physical signs of the disease are well known and do not require repetition, but the author mentions three clinical features which are not common but are striking when they occur: 1. Ocular symptoms probably occur more frequently than one would be led to believe. In their early stages they are characterized by pain in the eyes or pain back of the eyes which regresses during the second week but leaves the patient with puffy eyelids. 2. A papulomacular rash is an irregular symptom but one which has been emphasized by Tidy. The eruption is diffuse or patchy and generally limited to the trunk. It is difficult to describe it by any other term than morbilliform; in two of the author's cases it was classified by the attending physician as a "drug

rash." It may be preceded or accompanied by an enanthem consisting of petechiae on the soft palate. 3. Jaundice is another manifestation present in the second or third week of the disease. It is often definite and striking. A recent report from Sweden emphasizes its importance. Infectious mononucleosis is a benign condition which is self limiting in two or three weeks. However, it may be a long time (perhaps six months) before the glands return to normal size and a long time before the patient feels well again. So prominent is this postfebrile depression that in severe cases it seems to be part of the disease.

Iowa State Medical Society Journal, Des Moines

29: 1-46 (Jan.) 1939

*Certain Diseases Associated with Changes in the Circulating Leukocytes. C. C. Sturgis, Ann Arbor, Mich.—p. 1.
Use of Sulfanilamide in Otolaryngology and Ophthalmology. C. C. Jones, Des Moines.—p. 6.
Marginal Refractive Errors. O. L. Thorburn, Ames.—p. 11.
The Management of Glaucoma. T. L. McKee, Keokuk.—p. 14.
Lymphocytic Choriomeningitis in Iowa. W. H. Presnell, Charlotte.—p. 18.

Significance of Changes in Leukocytes.—Sturgis points out that a careful study of the circulating leukocytes yields valuable information concerning the diagnosis and prognosis of certain diseases, especially when this information is considered with other clinical data. In general, such knowledge is derived from a consideration of the number of leukocytes, the differential leukocyte count, the character of the nucleus as an indication of the maturity of the cell and certain abnormal changes which occur in the cytoplasm. Too much dependence should not be placed on single isolated observations, because repeated tests are desirable as a check on the accuracy of the estimations and because frequent determinations furnish data on which a curve may be constructed and this serves as a valuable indication concerning the general trend of any disease process. The author discusses the changes in the polymorphonuclear leukocytes in infection; infectious mononucleosis, agranulocytic angina, and the leukemias.

Journal Industrial Hygiene & Toxicology, Baltimore

21: 1-28 (Jan.) 1939

Determination of Acid Insoluble Matter in the Sputums of Silicotics. H. Civin, I. A. Schreier, G. Martello and J. D. Hardy, New York.—p. 1.
*Basophilic Aggregation Test Applied to Cement Workers. F. R. Holden and C. E. Ralston, Pittsburgh.—p. 5.
Metabolism and Retention of Lead in Growing and Adult Rats. J. B. Shields, H. H. Mitchell and W. A. Ruth, Urbana, Ill.—p. 7.
Case of Fatal Gas Poisoning in Welding in a Closed Tank. R. J. Wright-Smith, Melbourne, Australia.—p. 24.

Basophilic Aggregation Test in Cement Workers.—Holden and Ralston found a significant increase in the basophilic aggregation count in sixty-three workmen exposed for an average of more than eleven years to limestone, shale and cement dust. No pathologic change in the cells suggestive of plumbism was found. The average basophilic aggregation count of seventy-three fellow workmen who were not exposed to dust was approximately the same as the average of all the workmen employed in the dusty areas. No evidence was found to indicate that the increased stippled cell counts obtained by Lehmann from the Thuringian cement workers is paralleled by a similar increase in basophilic aggregation counts made on cement workers in the United States.

Journal-Lancet, Minneapolis

59: 1-36 (Jan.) 1939

Foreign Protein in Ocular Therapy. J. D. Alway, Aberdeen, S. D.—p. 1.
Submucous Lipoma of the Rectum. J. K. Anderson and W. A. Fansler, Minneapolis.—p. 4.
Problems in Diagnosis and Treatment of Cholecystic Disease. A. M. Snell, Rochester, Minn.—p. 7.
The Function of the Student Health Service in a Municipal University. L. W. Sander, Detroit.—p. 11.
The Modern Use of Peroral Endoscopy. L. R. Boies, Minneapolis.—p. 14.
The Rating of Industrial Disabilities. R. M. Burns, St. Paul.—p. 17.
The Hard of Hearing Problem in a Student Health Service. M. M. Rossman and L. M. Hickernell, Syracuse, N. Y.—p. 20.
Old Tuberculin and Purified Protein Derivative of Tuberculin: Comparative Study as Reviewed from Recent Literature. I. Kerlan, Ashland, Ky.—p. 22.
Basal Anesthesia with Sigmodal: Preliminary Report. S. G. Schmidt, Chicago.—p. 26.

Journal of Nervous and Mental Disease, New York

89: 1-132 (Jan.) 1939

Vitamin B Deficiency and Nervous Diseases. F. H. Lewy, Philadelphia.—p. 1.
Pattern Features and Constitutional Susceptibility, as Related to Organic Brain Disease, with Special Reference to General Paralysis. Beatrice Postle, Columbus, Ohio.—p. 26.
Feelings of Unreality and Displacement: Preliminary Study. Annette C. Washburne, Milwaukee.—p. 37.
Difficulties in Differential Diagnosis of Brain Tumor in Older Age Groups. D. W. Hastings, Philadelphia.—p. 44.
*Hydration Studies in Epilepsy. E. Ziskind, Esther Somerfeld-Ziskind and Ruth Bolton, Los Angeles.—p. 52.
Tumor of the Left Lateral Ventricle with Mental Symptoms. S. W. Gross, New York.—p. 66.

Hydration Studies in Epilepsy.—The Ziskinds and Bolton draw certain deductions relative to dehydration therapy in epilepsy from the study of sixteen epileptic patients and nine normal subjects who drank, after an overnight fast, 7,000 cc. of tap water at a uniform rate of 1,000 cc. each half hour. Body weight, urinary output and specific gravity were recorded at intervals of thirty minutes. Convulsions followed hydration in half of the epileptic patients. There were no convulsions in the nine normal subjects. Blood dilution and water retention were greater in the epileptic than in the nonepileptic subjects. This observation, if substantiated, may have important bearing on the question of increased cell permeability in epilepsy. Blood dilution and water retention were greater in epileptic patients having seizures subsequent to hydration than in those not so affected. Although excessive amounts of water were a positive factor in precipitating seizures, average amounts did not have this effect. The results cast doubt on the efficacy of dehydration in controlling convulsions.

Maine Medical Journal, Portland

30: 1-20 (Jan.) 1939

Important Considerations in Serum Treatment of Pneumococcic Pneumonia. F. T. Lord, Boston.—p. 1.
Impressions Gained from Recent National Health Conference in Washington. W. F. Braasch, Rochester, Minn.—p. 7.
Advantages and Disadvantages of Graduate Nursing in Small Hospitals. Margaret A. Hebert, Gardiner.—p. 12.
Gunshot Wound of Pregnant Uterus: Report of Case. R. W. Belknap, Damariscotta.—p. 13.

Medicine, Baltimore

17: 381-518 (Dec.) 1938

The Coagulation of the Blood. P. Nolf, Brussels, Belgium.—p. 381.
*Plasma Fibrinogen Response in Man: Influence of Nutritional State, Induced Hyperpyrexia, Infectious Disease and Liver Damage. T. H. Ham and Fanny C. Curtis, Boston.—p. 413.
Sedimentation Rate of Erythrocytes: Influence of Technical, Erythrocyte and Plasma Factors and Quantitative Comparison of Five Commonly Used Sedimentation Methods. T. H. Ham and Fanny C. Curtis, Boston.—p. 447.

Plasma Fibrinogen Response in Man.—Ham and Curtis investigated the effect of nutritional deficiency and of protein feeding on the fibrinogen level in man and compared the fibrinogen response to artificial fever. The plasma fibrinogen response is compared to the variation in serum proteins, leukocytes and body temperature. Their conclusions are that: 1. The plasma fibrinogen concentration in normal human subjects is relatively constant for any one individual and is not significantly influenced by the conditions of fasting, ingestion of food, rest and short violent exercise. The limits of concentration observed for normal adult men and women are from 190 to 330 mg. per hundred cubic centimeters of plasma, with an average level of approximately 250 mg. 2. In uncomplicated and untreated cases of pernicious anemia in which dietary protein has been inadequate, the fibrinogen concentrations vary from below normal to normal levels with a lower average concentration than that of healthy subjects. 3. Nutritional deficiency in pernicious anemia, in scurvy and in pellagra does not prevent an increase of fibrinogen above normal in the presence of infection. 4. In normal subjects the daily ingestion of animal protein produces a moderate fibrinogen response, usually within normal limits. 5. Remission from pernicious anemia does not result in an increase of plasma fibrinogen when the diet is deficient in protein but is accompanied by an increase of fibrinogen to normal when the diet contains 50 Gm. of protein daily. 6. Fever induced by high environmental tem-

perature causes either no elevation or only slight and irregular elevation of plasma fibrinogen, whereas the intravenous injection of typhoid vaccine causes both fever and a significant and prolonged elevation of the fibrinogen level. Therefore fever probably is not the only cause of the abnormally increased concentrations of fibrinogen observed in many febrile diseases. 7. In infectious disease the fibrinogen response may be independent of the temperature and the leukocyte changes and may occur despite a failure of the leukocyte response. 8. A failure of fibrinogen to increase above normal in instances of severe infection may be a poor prognostic sign and may suggest the presence of significant hepatic damage even though clinical signs of disease of the liver are lacking.

Michigan State Medical Society Journal, Lansing

37: 1053-1148 (Dec.) 1938

The Management of Various Types of Colitis. J. A. Bargen, Rochester, Minn.—p. 1067.
Correlation of Clinical and Laboratory Data in Diseases of Lymph Nodes. R. Isaacs, Ann Arbor.—p. 1072.
Lymph Gland Removal in Cancer of the Cervix: Technic and Results. F. J. Taussig, St. Louis.—p. 1074.
Hearing and Deafness. O. V. Batson, Philadelphia.—p. 1078.
Low Ileum Intussusception Caused by Meckel's Diverticulum: Report of Case. J. Johns, Ionia.—p. 1083.
Latent Lobar Pneumonia. J. Freedman, Detroit.—p. 1084.
Roller Skate Ambulatory Treatment of Fracture of the Patella. Nina C. Wilkerson, Sturgis.—p. 1086.
Prolapse of the Uterus. J. L. Baer, Chicago.—p. 1089.
The Injection Treatment of Hernia. F. A. Kelly, Detroit.—p. 1095.
The Educational Value of Our Student Health Services. I. W. Sander, Detroit.—p. 1098.
Influence of Disease on History. E. A. Wishropp, Detroit.—p. 1101.
Quartan Malaria: Case Report. E. O. Jodar, Detroit.—p. 1111.
Office Secretary's Psychology with Patients and Visitors. H. C. Black, Battle Creek.—p. 1112.

Nebraska State Medical Journal, Lincoln

24: 1-40 (Jan.) 1939

A Practitioner's Point of View of Poliomyelitis. J. Zahorsky, St. Louis.—p. 1.
*Deficiency and Nutritional Disorders in Etiology and Treatment of Cardiac Disease. F. W. Niehaus and W. D. Wright, Omaha.—p. 4.
Automatic Birth Control. C. R. Spicer, Hastings.—p. 9.
Study of Twenty-Two Cases of Hemolytic Jaundice and Effect of Splenectomy. J. C. Sharpe, Omaha.—p. 10.
Pulmonary Emphysema in Acute Respiratory Infections. E. Korol and H. A. Scott, Lincoln.—p. 15.
Surgical Complications in Pregnancy: Six Case Reports. E. C. Sage, Omaha.—p. 19.
Analysis of 150 Cases of Carcinoma of the Rectum, Anus and Rectosigmoid. L. E. Moon, Omaha.—p. 22.
Nodular Cirrhosis of Liver: Case Report. J. C. Eagan, Madison.—p. 28.

Deficiency Disorders in Heart Disease.—Niehaus and Wright consider the influence of various nutritional and deficiency states in connection with heart disease. The chief complaints of persons with cardiac disorders are referable to the gastrointestinal tract, at least sharing equal mention with the respiratory system. At present vitamin B_1 appears to be the only one of the vitamins having important cardiovascular influence. With regard to the heart it seems significant that the myocardium is richly supplied with vitamin B_1, being exceeded only by the liver and kidneys (Cowgill). This would seem to indicate an increased need rather than a storage place. Jones and Sure reported marked improvement in heart disease in patients receiving daily from 1,500 to 2,200 units of vitamin B. Their analysis, however, is not entirely convincing. Obesity has long been recognized as a handicap to the cardiovascular system. The very common occurrence of breathlessness with overweight is evidence that this condition imposes a circulatory load which is met with some difficulty. In addition to the local deleterious effect of deposition of fat around and within the wall of the heart, fat deposits in the rest of the body demand extra cardiac effort. While many other etiologic factors causing heart disease are obscure and difficult to influence, the factor of obesity offers a method by which these diseases may be prevented or, if present, more favorably influenced. The gratifying fall of blood pressure with weight reduction is a common experience. Undernutrition may be a factor in cardiovascular disease. This, unless very marked, usually does not have an important part in the cause of heart disease. Only with extreme wasting of the skeletal muscles is the weight of the heart reduced from 20 to 50 per cent. But more often it is a factor in heart disease due to other etiologic agents, such as is manifested in cardiac cachexia. This disorder has been considered a toxemia but is more probably a deficiency state. This is frequently attended by anemia and hypoproteinemia. These factors prevent proper nourishment of the myocardium as well as of the rest of the body. A low intake of proteins or protein sparing foods as carbohydrates may be factors in impoverishing the blood. Besides this a deficient intake of vitamins B and C may be further factors. Vitamin C deficiency may result in capillary damage and permit easy exit of the blood from the capillaries. Anemia also prevents adequate nutrition of the myocardium. Impoverished blood may not supply sufficient oxygen to the heart, which may result in an anoxemia manifested by a typical anginal syndrome. This may occur in anemia, particularly in the presence of a defective coronary vascular system.

New Jersey Medical Society Journal, Trenton

36: 1-68 (Jan.) 1939

The Present Status of Sulfanilamide Therapy. T. K. Lewis, Camden.—p. 5.
Treatment of Infections of Central Nervous System, with Special Reference to Sulfanilamide. Josephine B. Neal, New York.—p. 8.
Roentgen Therapy of Cancer by the Method of Chaoul. G. T. Pack, New York; J. S. Gallo and B. F. Wilkinson, Paterson.—p. 15.
Bilateral Cavernous Sinus Thrombosis, Recovery Without Operative Intervention: Report of Case. H. D. Barnshaw, Camden.—p. 22.
Presenting Multiple Areas of Enteritis: Report of Case. G. Blackburne, Newark.—p. 24.
Health Maintenance in Industry. C. D. Selby, Detroit.—p. 26.

New York State Journal of Medicine, New York

39: 1-100 (Jan. 1) 1939

The Significance of Hoarseness. V. E. Negus, London, England.—p. 9.
Relation of Diabetes to Surgery. I. Abell, Louisville, Ky.—p. 13.
Diet and Dental Caries. R. W. Bunting, Ann Arbor, Mich.—p. 18.
*Type III Pneumococcus Pneumonia: Effect of Para-Aminobenzenesulfonamido Pyridine in Treatment. E. A. Lawrence, New York.—p. 22.
Blood Culture: Aid in Determining Type in Lobar Pneumonia: Not on Sulfanilyl-Sulfanilamide in Type III Lobar Pneumonia and Septicemia. R. D. Roecker and J. Millett, New York.—p. 26.
Tonics and Sedatives in Neurologic Practice. H. S. Howe, New York.—p. 31.
Benzedrine Sulfate Therapy: Present Status. E. C. Reifenstein Jr. and E. Davidoff, Syracuse.—p. 42.
The Tryptophan Reaction: Aid to Early Diagnosis of Meningeal Tuberculosis. J. A. Buchanan and H. Ballweg, Brooklyn.—p. 58.
Surgical Treatment of Diseases of the Colon. T. E. Jones, Cleveland.—p. 60.
Outline of Treatment for Syphilis: Methods and Technic Followed in the Department of Dermatology of the Vanderbilt Clinic: Part I of a Series. A. B. Cannon, New York.—p. 70.

Type III Pneumococcus Pneumonia.—Lawrence used sulfapyridine in the treatment of two cases of type III pneumococcus pneumonia. Both patients recovered and the crisis occurred with rapid abatement of symptoms. Recovery was uneventful. Both patients were men more than 65 years of age, both were addicted to alcohol, and hypertension, auricular fibrillation and chronic bronchial asthma complicated the picture. Crisis occurred after only a small quantity (respectively 4 and 10 Gm.) of the drug had been administered, possibly demonstrating the direct action of the drug on the invading organism regardless of the concentration of the drug in the blood (the initial dose was respectively 1 and 2 Gm.). The only untoward symptoms produced by the drug were nausea, hiccuping and mild cyanosis, all of which rapidly cleared on cessation of the drug. The toxicity of the drug appears to be much less than that of sulfanilamide. Bacteriologically, in the reported cases, the main action of the drug is first to cause the loss of type specificity of the pneumococcus, which is then followed by complete decapsulation of the organism and finally by its inability to grow either on artificial mediums or in the mouse's peritoneum. It seems that there is a definite bacteriostatic action since improvement is observed so early in the disease. On mouse passage the reverse process is observed: first the reappearance of the capsule and second the reestablishment of type specificity. There was no demonstrable change in the type of the original organism in spite of the complete decapsulation and mouse passage.

Pennsylvania Medical Journal, Harrisburg

42: 337-464 (Jan.) 1939

The Control of Pneumonia. M. Finland, Boston.—p. 349.
Therapeutic Aspects of Cardiac Pain. R. L. Levy, New York.—p. 361.
The Follow-Up Treatment of the Ambulatory Cardiac Patient. W. G. Leaman Jr., Philadelphia.—p. 365.
New Thoughts on Diabetes. E. L. Bortz, Philadelphia.—p. 374.
Pathologic Physiology and Pathology of Diabetes Mellitus: Consideration of the Important Recent Discoveries. S. Warren, Boston.—p. 376.
Irradiation of Cutaneous Manifestations of Lymphoblastoma. R. G. Pett, Pittsburgh.—p. 387.
Treatment of Tuberculosis of the Bladder. L. F. Milliken, Philadelphia. —p. 392.
Use of Analgesia During Labor and Delivery. R. E. Nicodemus, Danville.—p. 395.
*Sinusitis in Children. A. B. Miller, Pittsburgh.—p. 399.
Edema: Its Differentiation and Treatment. R. R. Snowden, Pittsburgh. —p. 403.

Sinusitis in Children.—Miller declares that every acute cold is potentially an acute sinusitis. In children the acute exanthems, especially measles and scarlet fever, are often accompanied by severe acute sinusitis, which later leads to chronic involvement of the sinuses. Silverman reports an x-ray study of 300 cases of scarlet fever, 91 per cent of which showed definite sinusitis during the disease. The child who is undernourished, who has poor hygienic surroundings or an inadequate diet or who has some underlying constitutional condition is more apt to develop acute sinusitis just as he is more likely to develop chronic sinusitis. Anything which causes mechanical obstruction to normal nasal aeration and ventilation is another predisposing cause. The exciting causes are acute catarrhal fevers, acute exanthems, swimming and diving. Home treatment as a rule is sufficient in acute sinusitis and usually falls to the lot of the pediatrician or family practitioner. Adequate ventilation and drainage are important and should be accomplished by frequent use of astringent drops or sprays. Frequent use of inert liquid petrolatum drops in young children is contraindicated because of the danger of producing pneumonia. Only in the presence of some grave complication should any surgical procedure be undertaken in acute sinusitis and it should be as conservative as possible. The simple drainage of a subperiosteal collection of pus by incision through the periosteum is usually adequate. The ethmoidal labyrinth should never be attacked by the intranasal route in childhood because the possibility of meningitis is too grave. Osteomyelitis requires extensive surgical removal of bone. Unfortunately too many cases of acute sinusitis pass insidiously to the subacute and chronic state, the patients being discharged as cured. The prognosis of chronic sinusitis in children is better than in adults provided proper treatment is given. Treatment should be persisted in over a considerable period and a child should be observed periodically for several years before he is discharged as cured of chronic sinusitis.

Philippine Islands Med. Association Journal, Manila

18: 751-818 (Dec.) 1938

Pregnancy in Uterus Duplex: Report of Three Cases. Honoria Acosta-Sison and J. R. Katigbak, Manila.—p. 751.
Present Status of Therapeusis in Pulmonary Tuberculosis. M. Quisumbing, San Pablo, Laguna.—p. 759 .
Further Studies of Sulfanilamide. J. Y. Fores, Manila.—p. 765.

Public Health Reports, Washington, D. C.

54: 1-28 (Jan. 6) 1939

The Health of the Nation. T. Parran.—p. 1.
*Nonindustrial Injuries Among Male and Female Industrial Employees. H. P. Brinton.—p. 6.

Nonindustrial Injuries.—Brinton reviews the data on nonindustrial injuries and sickness causing disability for eight consecutive days or longer reported to the United States Public Health Service by industrial sick benefit organizations. Examination of these reports shows a small but consistent excess in the rate of nonindustrial injuries among female industrial employees for all companies and for eleven companies which reported to the United States Public Health Service for the entire period 1925 through 1937. For one company an analysis of all nonindustrial injuries which lasted eight days or longer revealed that the difference between the male and female rates was largely due to a relative excess among women of injuries to the lower extremities and injuries to multiple parts of the body. The frequency of injuries was shown to vary according to age as well as to sex. The injuries were found to be less serious among women than among men, while the average number of days lost per person was slightly greater for the former. When a company which reported disabilities lasting from one to seven days inclusive was selected, the relative excess of women became considerably greater. It appears from this study that, for the companies reporting, women were absent from work more often and for a longer time because of nonindustrial injuries than were men. This does not necessarily indicate that women are more prone to such injuries, as other factors, such as a different psychologic attitude toward injuries or a different attitude toward regularity of attendance at work, may play a part. The type of injury was classified in 86.6 per cent of the male injuries and in 85.4 per cent of the female injuries. Assuming that the unknown injuries are evenly distributed, it would appear that women had relatively fewer fractures than men but more sprains, cuts, bruises and burns. The proportion that fractures bear to all types of injury increased slightly with advancing age. There was an apparent tendency for the difference between the male and female percentages to be less in the older age period with respect to sprains and more with respect to burns, cuts and bruises.

Rhode Island Medical Journal, Providence

22: 1-18 (Jan.) 1939

Early versus Late Operations in Acute Cholecystitis. A. V. Migliaccio, Providence.—p. 1.
The Role of the Pathologist in the Cancer Problem. B. E. Clarke, Providence.—p. 4.
The Role of the Radiologist in the Cancer Problem. I. Gerber, Providence.—p. 6.

Rocky Mountain Medical Journal, Denver

36: 1-72 (Jan.) 1939

*Serum Therapy in Pneumococcic Pneumonia and Reduction in Pneumonia Mortality. C. D. Head Jr., Washington, D. C.—p. 18.
Common Forms of Diarrhea and Their Management. J. A. Bargen, Rochester, Minn.—p. 23.
Vaginal Hysterectomy and Its Indications. J. W. Kennedy, Philadelphia. —p. 29.
Air Injection for Diagnosis of Brain Disease. P. R. Weeks and J. K. Orr, Denver.—p. 33.

Reduction of Pneumonia Mortality by Serum Therapy.—Head points out that the need for all possible speed in the bacteriologic diagnosis and serum treatment of pneumonia is clearly shown by the lower mortality when this treatment is begun early after onset. The sooner serum is given after onset, the lower will the mortality be. Pneumonia is a medical emergency just as acute appendicitis is a surgical emergency. The physician who waits for dulness, bronchial breathing and other signs of consolidation to appear before making a diagnosis of pneumonia has allowed the most propitious time for treatment to pass. The patient who suddenly develops chills, pain in the side, cough with rusty sputum and fever should be considered to have pneumonia until proved otherwise. Failure of a patient to respond to serum after from twelve to eighteen hours calls for a complete bacteriologic restudy of the case; that is, typing of the pneumococcus and a culture of the blood. It has occasionally happened that a patient has received serum of a type corresponding to the organism found in his sputum, without favorable response, and a culture of his blood showed a pneumococcus of a different type.

Virginia Medical Monthly, Richmond

66: 1-64 (Jan.) 1939

Effects of Protracted and Recurrent Congestive Heart Failure on the Liver. F. A. Willius, Rochester, Minn.—p. 1.
The Problem in Caring for the Mentally Sick in Virginia. R. F. Gayle Jr., Richmond.—p. 6.
The Syphilis Problem in Roanoke. W. W. S. Butler, Roanoke.—p. 12.
Treatment of Benign Rectal Stricture (Lymphogranuloma Venereum). H. J. Warthen, Richmond.—p. 20.
Sulfanilamide, with Report of Treatment of Case of Puerperal Septicemia. A. F. Robertson Jr., Staunton.—p. 24.
Diverticulitis of the Cecum: Case Report. J. S. Staley, Marion.—p. 25.
The Hygiene of Swimming. H. M. Taylor, Jacksonville, Fla.—p. 32.
Relation of the Veterinarian to the Medical Profession. W. H. Feldman, Rochester, Minn.—p. 36.
New Operation for Treatment of Salpingitis. P. Jacobson, Petersburg.—p. 42.
Sirenomelus: Case Report. C. W. Futney, Staunton.—p. 44.
Aniline Dye Dermatoconjunctivitis: Report of Case. W. F. Bryce, Richmond.—p. 47.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Brain, London

61: 339-464 (Dec.) 1938

Tumors of the Thalamus: Clinicopathologic Study. G. E. Smyth and K. Stern.—p. 339.
*Cortical Deafness Without Aphasia. W. E. Le G. Clark and W. R. Russell.—p. 375.
*Cerebral Subcortical Myelinopathy in Carbon Monoxide Poisoning. Y. K. Hsü and Y. L. Ch'eng.—p. 384.
Olfactory Allo Esthesia. J. D. Spillane.—p. 393.
Differences Between Experimental Rigidities in Cats. E. G. T. Liddell. —p. 402.
Observations on Nervous Release. E. G. T. Liddell.—p. 410.
Deformity of the Hindbrain Associated with Internal Hydrocephalus: Its Relation to Arnold-Chiari Malformation. A. A. McConnell and H. L. Parker.—p. 415.
Familial Neuromyelitis Optica: Its Occurrence in Identical Twins. D. McAlpine.—p. 430.
Disturbances of Sensibility in Dystrophia Myotonica. O. Maas.—p. 449.

Cortical Deafness Without Aphasia.—Since Henschen (1918) collected sixteen cases of cortical deafness which up to that date had been reported with postmortem examination, Bramwell (1927) and Misch (1928) have each reported a further case. Now Clark and Russell present a case unlike other recorded cases in that the lesions were both subcortical and were so limited that there was no associated aphasia.

Myelinopathy in Carbon Monoxide Poisoning.—Hsü and Ch'eng made postmortem examinations of three cases of carbon monoxide poisoning. One of these showed typical bilateral hemorrhagic softening in the globus pallidus with no significant changes in the white matter and two presented diffuse changes in the deeper cerebral white substance. Clinically these two cases belong to the so-called relapsing type; that is, secondary changes appeared after recovery from the initial disturbances. One of these patients presented symptoms of catatonia and parkinsonism and died four months after the poisoning. In the other patient bronchopneumonia and empyema developed and he died four weeks later. Both brains showed a more or less diffuse degeneration of the white matter with progressive changes of glia cells and patches of demyelinization. There was no bilateral softening of the globus pallidus. A direct influence of the poison, or its anoxemic effect on the nervous tissue, is emphasized as a prominent pathogenic factor in these cases.

British Medical Journal, London

2: 1351-1402 (Dec. 31) 1938

Ulcerative Colitis: Clinical Aspects. E. R. Cullinan.—p. 1351.
*Id.: Personality Studies. E. Wittkower.—p. 1356.
Apical Bronchogenic Carcinoma. D. Owen, T. F. Hewer and P. H. Whitaker.—p. 1360.
*Outbreak of Sonne Dysentery. C. J. Trimble and W. C. V. Brothwood. —p. 1365.
Rheumatic Headache. J. Cyriax.—p. 1367.

Ulcerative Colitis.—Wittkower observed, from the psychologic point of view, forty unselected cases of ulcerative colitis. In thirty-seven cases psychologic abnormalities and disorders, far beyond the range of individual differences in the average population, were found to antedate the initial onset of the colitis. A dated clinical and life history, taken independently and verified by relatives, showed that disturbing events in the patient's life had preceded the onset, return and increase of symptoms more often than can be due to chance. Almost all the patients showed character disorders, obvious neuroses or psychoses. Seventeen patients who were overconscientious, overscrupulous, too orderly, most particular in cleanliness, obstinate and the like had obsessions. Twelve, characterized by emotional lability, temper tantrums, childishness, self centeredness and suggestibility, had hysterics. A group of six patients less well defined than the others contained some schizothymes and depressives. Five patients could not be grouped. The precipitating conflict situations, although fairly uniform within the various groups, showed no universally common similarities. If the relative significance of somatic and psychologic factors in the etiology of ulcerative colitis is assessed, little can be said in favor of a primary bacteriologic or dietetic origin. The psychologic factor seems the most constant cause. The riddle of the etiology of ulcerative colitis is still far from being solved. The psychologic background described is not necessarily the cause of the obscure disorder but it is certainly an important factor in the disease. Many problems in relation to the physical and psychologic aspects of the disorder await discovery. The observations appear to justify an attempt at psychotherapy for selected early cases of ulcerative colitis.

Sonne Dysentery.—Trimble and Brothwood report an outbreak of Sonne dysentery due to contaminated milk. It was not found possible to determine the source from which the milk became contaminated. Administrative action was followed by a prompt cessation of the outbreak, except for two "secondary" cases, which illustrates that instructions were not carried out faithfully. The outbreak demonstrates the importance of repeated examination of the feces of those infected if secondary cases are not to occur through a person's ignorance of the fact that he is still excreting the organism long after he appears to have recovered. It is particularly important that repeated examinations should be made of the persons actually handling milk and that they should be scrupulous in their personal cleanliness. The milk was supplied to twenty-four households, but only twelve were affected by the outbreak. Eighty-six persons partook of the milk incriminated in the outbreak, but only twenty-one became ill.

Medical Journal of Australia, Sydney

2: 1061-1102 (Dec. 24) 1938

The Public Health Laboratory in Relation to the National Health Service. H. A. Woodruff.—p. 1061.
Streptococcic Pharyngitis and Its Complications. F. V. Scholes.—p. 1065.
Chaoul Therapy: Specialized Form of X-Ray Treatment. E. W. Frecker. —p. 1077.

New Zealand Medical Journal, Wellington

37: 313-372 (Dec.) 1938

The Work of the Mayo Clinic. M. A. Falconer.—p. 316.
Polycythemia: Account of Five Cases. G. H. Robertson.—p. 328.
*Prevention of Paralytic Ileus. J. Cairney.—p. 334.
Treatment of Yaws Studied Serologically. G. Dempster.—p. 338.

Prevention of Paralytic Ileus.—In his discussion of the prevention of paralytic ileus, Cairney does not include the ileus due to peritonitis. Prophylaxis at operation (laparotomy) consists principally in the avoidance of every form of unnecessary trauma. In the postoperative prevention of paralytic ileus the author advocates that for the first forty-eight hours the patient be given from one-sixth to one-fourth grain (0.01 to 0.016 Gm.) of morphine as necessary for the relief of pain and restlessness, but not more often than every four hours. On the third morning the abdomen should be examined with a stethoscope. If audible peristalsis is present an enema is ordered, and if the result is satisfactory any suitable aperient may be given in just sufficient quantity to ensure a daily action of the bowels. If on the third morning audible peristalsis is absent and distention is commencing, prostigmine and acetylcholine are administered, followed by an enema. In some cases this is all that is necessary; in others the prostigmine and acetylcholine are repeated at intervals as indicated and radiant heat is applied to the abdomen. In these cases the occasional administration of morphine may have to be continued but is generally required only at night to ensure adequate rest. If on the third morning peristalsis is not audible but there is no sign of abdominal distention, the choice lies between delaying the administration of the enema, on the assumption that peristalsis will be in evidence some hours later, and the administration of prostigmine and acetylcholine. In no case is an aperient administered until a satisfactory result has been obtained from an enema. Each patient must be treated individually.

South African Medical Journal, Cape Town

12: 903-938 (Dec. 24) 1938

Treatment of Malaria in the Transvaal. S. Annecke.—p. 905.
Venereal Affections of the Anus and Rectum. L. F. Freed.—p. 909.
Proseptasine in Treatment of Gonorrhea. D. Landau.—p. 917.
Scurvy in Namaqualand. J. Henson.—p. 918.
The Injection Treatment of Hernia. W. P. Steenkamp.—p. 919.
Recent Advances in the Investigation of Peripheral Vascular Disease. C. F. M. Saint.—p. 922.
Backward Displacements of the Uterus. E. C. Crichton.—p. 923.

Archives des Maladies de l'Appareil Digestif, Paris

28: 1041-1164 (Dec.) 1938. Partial Index

*Splenoperivisceral and Spleno-Ulcerous Syndrome: Extrasplenic Lesions in Course of Splenomegalies Called Pylethrombosis. J. Caroli, P. Guérin and L. Scalfi.—p. 1051.
Lipomas of Cecum. R. Didier.—p. 1070.
Late Gastric Ulcer: Case. N. D. Hoang.—p. 1078.

Splenoperivisceral and Spleno-Ulcerous Syndrome.—Caroli and his associates direct attention to two anatomoclinical syndromes which may be associated or occur isolated: the splenoperivisceral syndrome and the spleno-ulcerous syndrome. In the splenoperivisceral syndrome the adhesions around the digestive tract coexisting with the splenomegaly may be limited to the duodenal bulb, or in other cases they may extend over the entire abdomen. One of the cases described in this report is of a hitherto unreported instance of association of hepatosplenic cirrhosis of undetermined origin and of ulcer of the duodenum. The fatal digestive hemorrhages which complicated this case seemed to be due to rupture of varices of the cardia. This case raises the question whether the involvement of the peritoneum is not perhaps the cause of the splenomegaly rather than an associated or secondary complication. Regarding the spleno-ulcerous syndrome, the authors say that they do not believe that this syndrome is purely coincidental but that it is probably grafted on the organic and functional alterations of parasplenomegalic gastritis. In one of the cases the muscular hypertrophy of the gastric wall demonstrated clearly what severe changes may be located in the stomach. Without doubt, they explain to a considerable extent the frequent postoperative persistence of hemorrhagic accidents. On the basis of two observations, the authors were able to show that the coexistence of ulcerous complications are of interest in relation not only to the spleen but likewise to the hepatosplenic cirrhoses, which may or may not be of alcoholic origin.

Journal Belge de Neurol. et de Psychiat., Brussels

38: 903-974 (Dec.) 1938

Regulation of Cerebral Circulation. J. J. Bouckaert.—p. 903.
*Is Parkinsonian Tremor Synchronous or Asynchronous? R. Nyssen, R. Busschaert and R. Dellaert.—p. 913.
Tumor of Benign Appearance in Gasserian Region. E. Evrard.—p. 918.
Anatomoclinical Study of Case of Postvaccinal Encephalitis. P. Van Gehuchten and M. Falcon.—p. 932.
Pathogenic Consideration of Certain Forms of Schizophrenia in Asthenic and Dysplastic Persons in Connection with Case of Acromicria, Tremor of Head and Lactic Secretion. M. Cahane and Tatiana Cahane.—p. 942.

Nature of Parkinsonian Tremor.—Nyssen and his associates say that in the course of previous investigations relative to certain clinical characteristics of parkinsonian tremor and to the influence of certain factors on the amplitude and frequency of this tremor they observed in a considerable number of subjects that the members do not tremble in a synchronous manner. Since this observation was in disagreement with the opinions of other observers, the authors decided to investigate this problem systematically. They studied fifteen patients with paralysis agitans and thirty patients with encephalitic parkinsonism. The tremor was registered by means of the mechanographic method. For a comparison of the frequencies of the tremor in two symmetrical homolateral or crossed members, the registration was always made simultaneously. The differences of the frequencies of two members were expressed in percentages. For instance if, during a period of ten seconds, the right hand registered fifty oscillations and the left hand sixty, it was said that the tremor of the left hand is 20 per cent more rapid. To the question whether there is synchronism in parkinsonian tremor, the authors reply that among their forty-five patients they detected a single case of relatively stable synchronism between two limbs. This patient presented identical frequencies in the right hand and the right foot. However, a comparison of the frequency of the right members with those of the left members presented the same asynchronism found in the majority of patients. The asynchronism observed in the other forty-four patients varied between 30 and 100 per cent. Further the authors investigated whether the degree of asynchronism differed according to whether the compared members were symmetrical, homolateral or crossed. The detected averages do not indicate this, but in some subjects the asynchronism of the tremor was more pronounced in the symmetrical members, in others more in the homolateral or crossed members. The authors intend to continue their studies in order to detect the factors that will explain the asynchronism in parkinsonian tremor.

Journal de Médecine de Lyon, Lyons

20: 1-34 (Jan. 5) 1939

*Duration and Degree of Immunity Conferred by Different Antityphoid-Paratyphoid Vaccines. J. Chalier and J. Ledru.—p. 1.
Typhoid in the Vaccinated. J. Chalier and J. Ledru.—p. 9.
Treatment of Pneumococcic Angina and Stomatitis by Local Application of Sterilized Oxbile. J. Chalier and J. Ledru.—p. 13.
Superficial Adenopathies in Course of Measles and German Measles. J. Chalier, L. Revol, J. Viaillier and A. Desbiez.—p. 19.

Antityphoid-Paratyphoid Vaccines.—Chalier and Ledru maintain that the value of antityphoid-paratyphoid vaccination cannot be denied. When it is administered by the subcutaneous route and in suitable doses it greatly diminishes the morbidity. However, they gained the impression that the different modes of vaccination are not all of the same value. They advise against the oral administration. The lipovaccines confer an immunity of short duration. The ether vaccine of Vincent produces the most reliable and the longest lasting immunity. The attacks of typhoid which developed in spite of this vaccination occurred mostly in subjects who had not been correctly vaccinated, not having received more than two injections. The heated TAB (triple) vaccine, especially when reduced to two injections, seemed less efficacious. Its immunizing power is of shorter duration and allows more refractory cases to persist. During the war and postwar years, typhoid in those vaccinated with ether vaccine was an extreme rarity. Less exceptional is typhoid of those vaccinated with heated triple vaccine, who may develop it as early as one or two years after the vaccination. The ether vaccine often provokes strong reactions, but these may be necessary for the development of a lasting immunity. The question therefore arises whether it might not be advisable to return to this mode of vaccination, with the multiplicity of injections which it requires but at the same time with reward of a reliable and lasting immunity.

Presse Médicale, Paris

47: 17-40 (Jan. 7) 1939

Sites of Origin of Ovarian Hormones: Hyperplasia of Endometrium as Test of Hyperestrinism. J. Wallart.—p. 17.
*Icterus in Diabetic Patients. P. Ducas and P. Uhry.—p. 19.

Icterus in Diabetic Patients.—Ducas and Uhry say that the concurrence of diabetes and icterus is less frequent than might be supposed. When the two disorders concur in persons over 50, the question arises whether it is merely a coexistence of diseases or a multiple manifestation of a complex diathesis. However, when the association occurs in children or young adults, the various factors that could be incriminated as possible causes of the icterus in old persons, such as alcoholism, lithiasis, malaria, syphilis and chronic intestinal intoxication, have not had time to develop or exert their effects and thus it is especially interesting to study the concurrence of diabetes and icterus in the young. The authors describe several cases of concurrence of diabetes and icterus in young persons. One patient was a man aged 22 who had had diabetes since the age of 14 and who developed a spirochetal icterus which led to an attack of acidosis and to a temporary decrease in the carbohydrate tolerance. Two other patients were boys aged 12 and 13 who had had diabetes for several years. In these cases the icterus was accompanied by hepatomegaly. The authors say that these histories reflect those reported by other authors. They show that the form and evolution of the icterus are little modified by the diabetic condition and that the aspects of icterus vary according to its etiology and are identical with those of nondiabetic persons. The only point which merits especial attention in the diabetic patients with icterus is the existence of an enlargement of the liver. This hepatomegaly may appear before the icterus or simultaneously with it. It may be slightly painful, but as a rule it is accompanied neither by ascites nor by splenomegaly. Generally it is transitory and disappears with the icterus; nevertheless it may persist for a long time, after the icterus has already disappeared.

Discussing the significance of this hepatomegaly, the authors show that it probably plays a part in the genesis of the icterus. In conclusion they stress that the icterus of diabetic persons, especially of young diabetic patients, does not have a uniform etiology, that it is comparatively rare and that the prognosis is as variable and as difficult to establish as is the case in nondiabetic persons. Its effect on the diabetes becomes manifest, as a rule, by a transitory aggravation of the diabetic disorder. The diet of these patients must be carefully watched; that is, the intake of fats should not be too high and that of sugars not too restricted.

Schweizerische medizinische Wochenschrift, Basel

69: 1-24 (Jan. 7) 1939. Partial Index

Clinical Aspects of Infectious Diseases. R. Staehelin.—p. 1.
Adequate and Inadequate Nutritional Preparations. E. Bürgi.—p. 7.
*Impairment of Heart in Tonsillitis. H. W. Hotz.—p. 10.
Ménière's Disease: Case. R. Guyot.—p. 12.

Impairment of Heart in Tonsillitis.—Hotz says that during the first part of 1938 tonsillitis assumed epidemic proportions at the medical clinic of the University of Zurich. The contagiousness of the tonsillitis was considerable; several room infections were observed and many of the nursing staff contracted it. Other unusual aspects of this epidemic of tonsillitis were frequent articular symptoms and electrocardiographic changes. It was decided to make electrocardiographic tests on all patients who had had inflammatory disorders of the tonsils, and abnormalities were observed in a surprisingly large number. It is noteworthy that if the occasional rhythmic disturbances are disregarded these electrocardiographically detectable disturbances often fail to cause clinical manifestations. The pathologic aspects of the electrocardiogram are usually transitory; moreover, they generally do not appear during the severest period of the disease but rather after the symptoms of sore throat and fever have already disappeared. As a rule there is no parallelism between the severity of the clinical aspects and the electrocardiographic disturbances, for severe electrocardiographic changes may appear in cases of tonsillitis that are comparatively mild and of short duration, and vice versa. The author cites and illustrates some of the electrocardiographic changes that he observed in acute cases of tonsillitis and says that other investigators observed similar changes during chronic tonsillitis and saw them disappear after tonsillectomy. In the concluding summary the author says that acute tonsillitis leads in a large percentage of cases (according to Otto in 60 per cent) to electrocardiographic changes which are probably the result of transitory, probably toxic, influences on the myocardium and the cardiac conduction system. Occasionally, myocarditic or coronaritic disorders may develop. The author admits that it would be unpractical to subject every patient with tonsillitis to electrocardiography; however, he emphasizes that physical exertion should be avoided during the period of convalescence and the patients should be carefully watched. Patients with chronic tonsillitis should be subjected if possible to electrocardiography, and tonsillectomy should be resorted to if pathologic changes are observed.

Giornale di Clinica Medica, Parma

19: 1683-1823 (Dec. 30) 1938. Partial Index

*Sign of Pain in Phrenic Nerve in Diseases of Abdominal Organs. C. Roncoroni.—p. 1683.
Vi Antigen of Bacterium Typhi. L. Soletta.—p. 1692.
Pernicious Anemia of Pretended Known Etiology. A. Terzani.—p. 1721.

Phrenic Nerve in Diseases of Abdominal Organs.—According to Roncoroni a reflex pain in the cervical point of the phrenic nerve (right supraclavicular fossa) is frequent in several diseases of the abdominal organs. It may be spontaneous or induced by palpation over the phrenic nerve on its passage on the anterior scalenus muscle (right supraclavicular fossa). The author investigated the presence of phrenic pain in 130 patients suffering from any of various diseases of the abdominal organs. He found that phrenic pain exists in all cases of diseases of organs in the right side of the abdomen and in pericholecystitis and cholecystitis both with and without calculi. The sign may be positive (presence of phrenic pain) in appendicitis (either acute or chronic), periduodenitis and duodenal ulcer whenever the cystic point is painful and not otherwise. It is negative (absence of pain) in both the right and the left sides, in gastric ulcer, in gastric cancer, in renal calculi and in pyelonephritis. According to the author the sign is of diagnostic value, showing pathologic conditions of either or both the gallbladder and the perihepatic peritoneum. He believes that pain in the phrenic nerve shows a reaction of irritability of the nerve to a direct involvement of its peritoneal branches in the local inflammatory process. Involvement of the peritoneal phrenic branches in the local pathologic process induces a painful reaction which is transmitted to the upper segments of the nerve.

Prensa Médica Argentina, Buenos Aires

25: 2437-2490 (Dec. 28) 1938. Partial Index

Hypovitaminosis in Clinical Diseases. M. R. Castex and M. Schteingart.—p. 2437.
*Alterations of Liver in Erythroblastic Anemia with Jaundice. M. Acuña and A. A. Bonduel.—p. 2444.
Treatment of Achylic Hypochromic Anemia. E. S. Mazzei.—p. 2453.

Liver in Erythroblastic Anemia.—According to Acuña and Bonduel, the liver becomes involved in the course of hemolytic erythroblastic anemia which results from the contact of the structure with hemoglobin from hemolysis. The lesion in the liver permits the passage of direct bilirubin to the blood with consequent development of jaundice with a clinical picture which is similar to that of hemolytic jaundice (Minkousky-Chauffard's type). The authors made a clinical study and tests for the function of the liver in several children and adolescents who were suffering from erythroblastic anemia with jaundice. They found that the patients have periodic aggravations which are controlled by transfusion. The crasis of the blood is that of intense anemia with presence of a large number of immature erythrocytes and leukocytes. Frequently the blood picture is that of von Jaksch's pseudoleukemia. The liver is enlarged. Material from the liver which is taken by a biopsy shows various alterations of the structure, especially acute infiltration with pigments derived from hemoglobin. The Kupffer cells of the liver are engorged with transformed hemoglobin. Serial tests for function of the liver show insufficiency, which depends on the intensity and evolution of erythroblastic anemia. It intensifies in the periods of deglobulization and improves during the periods of amelioration of anemia. The elimination of hippuric acid is diminished. Bilirubinemia and galactosuria are increased. Hyperbilirubinemia is indirect early in the development of the disease and direct as the latter progresses. Hunter and Harrison tests for bilirubin in the urine gave positive results. Urobilinuria is increased especially during the periods of deglobulization and in advanced phases of the disease. The authors therefore conclude that erythroblastic anemia with jaundice and congenital splenomegalic hemolytic jaundice (Minkousky-Chauffard's type) are two different clinical forms of congenital hemolytic jaundice.

Klinische Wochenschrift, Berlin

17: 1785-1824 (Dec. 17) 1938. Partial Index

Vitamin C Requirements and C Hypovitaminosis. Rietschel.—p. 1787.
*Carbohydrates and Minerals in Their Significance for Metabolic Disturbances of Pregnancy. H. Albers.—p. 1792.
Action of Vitamin D_2 and D_3 on Rickets and Spasmophylia. H. Bischoff and H. Brieger.—p. 1795.
Pathogenesis and Treatment of Bronchitis Fibrinosa. O. Roth.—p. 1798.
Dependence of Growth on Growth Hormone of Hypophysis and on Hormone of Thyroid. W. Albrecht and K. Fellinger.—p. 1801.
Quantitative Chemical Method for Determination of Mucin Content of Gastric Juice, Saliva and Sputum. J. Glass.—p. 1802.
Standardization of Thoracic Leads of Electrocardiogram: Remarks on Early Picture of Infarct of Posterior Wall and of Recurrent Infarct of Anterior Wall. W. Nehb.—p. 1807.

Carbohydrates and Minerals in Pregnancy.—Discussing the carbohydrate metabolism during pregnancy, Albers says that the blood sugar level is generally low during pregnancy. On the basis of a large number of metabolic tests it has been concluded that the glycogen fixation is reduced or that there is a considerable glycogenolysis. However, in spite of the low blood sugar content a tendency toward increased mobilization of the sugar can be demonstrated by means of sugar tolerance tests. The changes in the course of the carbohydrate metabolism are the result of the incretory changes of pregnancy. The anterior lobe of the hypophysis, the thyroid

and the adrenal system promote the contra-insular process. Some forms of glycosuria are not caused by insufficiency of the insular apparatus but rather by hyperfunction of the contra-insular system. The regulation by the incretory system of processes in the intermediate carbohydrate metabolism helps to explain conditions like alimentary and extra-insular glycosuria of pregnancy. The author stresses the importance of the differentiation between true diabetes mellitus and the extra-insular glycosuria of pregnancy. In the extra-insular glycosuria of pregnancy the blood sugar content is not related to the elimination; the sugar tolerance test produces normal results and the elimination of sugar is independent of the carbohydrate intake; moreover, the glycosuria is refractory to insulin therapy. If the examination of the pregnant woman who has glycosuria discloses true diabetes mellitus the customary dietetic and insulin therapy must be instituted, but if the glycosuria is of the extra-insular type treatment is either unnecessary or it is of a type exactly opposite to that of diabetes mellitus; that is, the pregnant woman must be given more carbohydrates than she eliminates so that the balance will be a positive one. During the later periods of pregnancy the glycosuria usually decreases and often disappears entirely. The author shows further that in some hepatic impairments of pregnancy carbohydrate therapy is advisable and that it promises favorable results also in hyperemesis gravidarum, severe dropsy of pregnancy, preeclampsia and eclampsia. In the course of a hyperemesis the urine of the patient should be examined from time to time for the presence of sodium chloride. If on addition to the urine of a 1 per cent solution of silver nitrate there appears a sediment of thick white floccules, hypochloremia is absent; but if the urine remains clear a sodium chloride deficiency of the blood must be suspected and searched for and the rest nitrogen content must be tested. The intravenous administration of sodium chloride increases the salt content of the blood and reduces the rest nitrogen. But although hypochloremia is so far the only disorder curable by mineral therapy the author thinks that the late toxicoses might perhaps be influenced indirectly by minerals.

Monatsschrift für Kinderheilkunde, Berlin

76: 305-444 (Dec. 15) 1938. Partial Index

Aspects of Congenital Deformities of Skeleton. Ilse Besdziek.—p. 305.
*Treatment of Atrophies in Nurslings with Extracts of Liver and of Posterior Lobe of Hypophysis. Anna von Szász and S. von Gárdos. —p. 322.
German Measles a Virus Disease. Y. Hiro and S. Tasaka.—p. 328.

Atrophies in Nurslings.—According to von Szász and von Gárdos the entire organism, including the incretory glands, are involved in atrophy of nurslings. The symptomatology of the atrophy differs, depending on which organ dominates the disease process with its atrophy. The authors observed some cases with symptoms of atrophy of the liver and of the posterior lobe of the hypophysis. After listing the characteristics of the normal liver in nurslings they mention the changes that develop during atrophy and then they discuss the treatment. They show that, in cases of grave atrophy with small liver, the hepatic function can be improved (1) by nourishment with foods that have comparatively high carbohydrate and sodium chloride contents; however, the tolerance must not be exceeded; (2) by the parenteral administration of solutions of sugar and of sugar and salt; (3) by feeding with vegetables that have a high vitamin content; (4) by injecting blood serum; (5) by intramuscular injections of liver extract, and (6) by the administration of liver, sugar and solution of posterior pituitary. As the size of the liver increases, the general condition and the tolerance improve. The administration of solution of posterior pituitary is indicated (1) in the severe forms of atrophy with polyuria and polydipsia, provided hydrostasis and edema are absent, (2) in Leiner's dermatitis and generalized eczemas, when it should be given in small doses during the erythematous stage until vasoconstriction results and (3) in cases of severe meteorism which result from intestinal paralysis and complicated toxic and septic disorders. However, the administration of solution of posterior pituitary is contraindicated in the forms of atrophy that are accompanied by vasoconstriction and edema.

Klinicheskaya Meditsina, Moscow

Pp. 1437-1604 (No. 11) 1938. Partial Index

Prophylaxis of Serum Disease. M. P. Kireev.—p. 1441.
Sweat Elimination. L. I. Vilenskiy.—p. 1446.
Pathogenesis of Colds. V. V. Petrovskiy, E. P. Chereshkevich and K. F. Berkgaut.—p. 1452.
*Early Diagnosis of Gastric Cancer. Ya. M. Bruskin.—p. 1463.
Diagnostic Errors in Cancer of Stomach. L. M. Nisnevich and A. N. Machabeli.—p. 1474.
Clinical-Roentgenologic Diagnosis of Cancer of the Cardia of the Stomach. S. L. Kopelman and I. L. Tager.—p. 1485.

Early Diagnosis of Gastric Cancer.—According to Bruskin, more than 50 per cent of the patients suffering from cancer of the stomach come to the surgical services or to the oncologic institutes in an advanced inoperable state. The mortality from gastric cancer in Moscow during the years 1929-1931 amounted to 40 per cent of the total mortality from malignant neoplasms. During the years 1926-1934, 250 cases of gastric cancer were treated at the Central Oncologic Institute of Moscow. The distribution according to sex was 60 per cent in men and 40 per cent in women. The histories of the majority of the patients revealed the existence of a long standing gastric complaint. This, in the opinion of the author, suggests an etiologic relationship between the preexisting states such as gastritis, ulcer and polyposis, and the subsequent cancer. The former may therefore be properly regarded as precancerous states particularly in patients beyond 40 years of age. The symptom complex of the early stage of the gastric cancer is frequently vague. Dyspeptic complaints, progressive emaciation and blood in the feces in a middle aged person are to be regarded as suggestive of gastric cancer. The author stresses particularly the value of the x-ray study of the mucosal relief in the early diagnosis. The proper procedure in doubtful cases is an exploratory laparotomy combined, when necessary, with a gastrotomy. Conservative waiting in such cases will clear the diagnosis but will rob the patient of a chance of recovery. The early recognition and treatment of inflammatory processes of the stomach (gastritides) in the middle aged is to be regarded as prophylaxis against later development of a blastomatotic process.

Acta Medica Scandinavica, Stockholm

97: 427-620 (Dec. 17) 1938. Partial Index

*Central Control of Metabolism of Fats. C. D. de Langen.—p. 427.
Diastolic Regurgitation Murmur Heard Near and At Apical Region of Heart in Uremia with Negative Necropsy Observations. H. A. Salvesen.—p. 440.
Studies on Case of Essential Levulosuria. Edhem, F. Erden and K. Steinitz.—p. 455.
Hyperergic, Transitory Infiltrations of Lung, Which Are Accompanied by Eosinophilia During Tuberculosis and Abortive Pneumonias. S. J. Leitner.—p. 473.
Normal Variations of Water Diuresis and of Water Tolerance Test. J. Möllerström and S. Forssman.—p. 508.
*Symptomatology of Acute Porphyria and Classification of Porphyrias. A. Eldahl.—p. 527.
*Polycythemia Treated with Roentgen Irradiation of Pylorus Organ. F. Andersen, T. Geill and E. Samuelsen.—p. 547.
Investigations on Effects of Nicotinic Acid on Two Patients with Idiopathic Steatorrhea (Sprue). J. Bing and B. Broager.—p. 561.

Central Control of Metabolism of Fats.—De Langen says that in a previous paper he pointed out that hyperlipemia not only accompanies anemia resulting from bleeding but also occurs when anemia is the result of injections of a hemolyzing substance. In both cases the fats and lipoids in the blood do not increase gradually in proportion as the hemoglobin content and the number of red blood cells decrease suddenly. If the anemia is not further increased, the fat curve rises as sharply as it previously dropped and becomes normal in the course of a few days. If the bleeding or the hydroxylamine injections are repeated, the same phenomenon is observed to occur at the same stage of the process. This rapid development of hyperlipemia gives the impression that it is under central control. A number of different methods have been applied in the effort to prove and localize this central control of the metabolism of fats. The author found that in rabbits which have been anemized about 50 per cent by one or other of the two processes mentioned and in which the spinal cord is cut between the third and fourth thoracic vertebrae, continued bleeding or injection of hydroxylamine does not elicit

hyperlipemia nor did it occur when the anemia was brought below 40 per cent. This absence of any increase in fats, which otherwise occurs regularly, suggests the possible existence of a central control. It was noted that lipemia can be induced in rabbits by the administration of sulfonmethane. After a highly lipemic serum had been observed in a patient with barbital poisoning, the author studied the effect of barbituric acid preparations and of other hypnotics on the fat content of the blood. It was found that the various hypnotics differ in their effect on the fat metabolism. Barbituric acid preparations have a narcotic effect on the mesencephalon and various experiments with narcosis of the mesencephalon demonstrated that the hypophysis is involved in the fat metabolism. Discussing the problem as to how the increase in the fat content of the blood is brought about, the author calls attention to the role of the liver. There are a number of indications suggesting that the liver plays a major part in the metabolism of fats. The varying composition of the fats contained therein lend great probability to this hypothesis. In hyperlipemia, such as was produced by artificial anemia and by mesencephalic narcosis, fat accumulated in great quantities in that organ. The sudden rising and falling of the blood fat in anemic hyperlipemia suggests a regulating mechanism of a neurogenic nature. The great increase of fat in the blood produced by the action of barbituric acids and certain other hypnotics strengthens the conviction regarding this central regulation. Observations also support the view that there must be a center in the mesencephalon that plays some part in the regulation of the metabolism of fats. The results of investigation of the influence exerted by the anterior and by the posterior lobe of the hypophysis justify the supposition that the latter gland affects the center both positively and negatively. The fact that the influence of this center on the metabolism of fats is inhibited when the spinal cord is cut at the third thoracic vertebra indicates that the necessary stimuli connected are transmitted to the abdominal organs by the nerve pathways communicating with it. Finally, the changes noted as taking place in the liver during hyperlipemia point to the liver as the central organ which, in response to a central regulating mechanism, brings about the metabolism of fats.

Porphyria and Classification of Porphyrias. — Eldahl differentiates forms of porphyrinuria without symptoms from those with symptoms. Discussing the group without symptoms, he mentions (1) the hereditary type, which may be either constant or periodic, (2) the symptomatic type, which is observed in fever, anemia and so on and (3) the medicamental type, which develops after medication with arsphenamine and with certain hypnotics. With the group of porphyrinurias which present symptoms, the author classes (1) the disorder that is designated as porphyria, (2) the toxic form, which is caused by arsenic, lead or hypnotics, and (3) hydroa vacciniforme. He gives especial attention to the entity known as acute porphyria. This is an acute disease with the following symptoms: violent abdominal pains, obstinate constipation (rarely diarrhea), organic illness of the cerebrum and the medulla (insomnia, psychoses, multiple pareses), hepatic and renal insufficiency, elimination of chromogen and porphyrin in the urine. The cause is supposed to be a congenital and severe abnormality in the intermediary metabolism, a latent or relative insufficiency of the porphyrin synthesis, which through some cause may become absolute. The synthesis probably takes in the liver. Eliciting causes may be infections, overwork, psychic trauma and chemicals in small amounts. The prognosis is unfavorable. An acute attack is often fatal. The mortality varies but it averages around 70 per cent. The disorder is most frequent in women (about 70 per cent of all cases); those between the ages of 20 and 30 develop it most often and have the highest mortality. Porphyria may run in families. It has been traced through three generations. Regarding the treatment, the author says that in many cases dietetic treatment has been employed, an innocuous diet, such as the one formerly used in hepatic and renal diseases. Some authors use diuretics. This, however, dos not seem justified when it is considered that edemas arc never seen in porphyria. This treatment seems to have augmented the existing toxic injury to the organs. Sodium carbonate has been tried, because the urine in porphyria is strongly acid. The author doubts that any effect has been obtained. Liver preparations have been used in many cases. The author employed the therapy which is now common in hepatic injuries and hepatitis, namely insulin and dextrose.

Polycythemia Treated by Irradiation of Pylorus. — Andersen and his associates point out that in 1931 Hitzenberger advanced the theory that pernicious anemia and polycythemia are diametrically opposite diseases, representing respectively the result of an underproduction and an overproduction of the intrinsic factor. In 1934 Hitzenberger advocated resection of the pylorus organ as being the only causal therapy in polycythemia, but he acknowledged that resection is advisable only in cases simultaneously involving a juxtapyloric ulcer. In two cases of polycythemia without ulcer, Hitzenberger tried roentgen irradiation of the stomach. In one case the hemoglobin (Sahli) dropped from 140 to 100 per cent, the red cells from 8.9 to 5.6 million. In the other case the hemoglobin fell from 128 to 110 per cent, the erythrocytes from 9.5 to 7 millions. The result, however, was not permanent, as the blood values rose again after a few months. Later Hitzenberger seems to have abandoned irradiation of the stomach and recommended universal roentgen irradiation of the body as proposed by Sgalitzer. When the authors began their investigations on polycythemia they were unaware of Hitzenberger's two cases. Based on Meulengracht's work on pernicious anemia they decided to try roentgen treatment of the isolated pylorus to obtain a diminution of the supposed overproduction of the intrinsic factor. This was regarded as more rational than the weakening of the bone marrow by irradiation of the entire osseous system. Discussing the technic of the roentgen irradiation, they say that the pyloric region can be reached through a cutaneous circular area, approximately 9 cm. in diameter. In order to locate the field, the patient is placed on the trochoscope in a position identical to the posture occupied during the subsequent irradiation, i. e. resting on the back and with the same number of cushions under the head. Slight movements or even deep breathing may result in considerable displacement of the field. The patient is given a small portion of a fluid contrasting agent and a few minutes later the region is observed by fluoroscopic examination. In order to locate the field on the abdomen, the authors devised a localizer consisting of a metal ring with a diameter of 9 cm. The ring was placed on the abdomen under the fluoroscope so that it circumscribed the pylorus and the descending part of the duodenum. After the fluoroscope has been removed the circumscribed cutaneous area is marked off with a colored pencil. First the authors gave a series of four irradiations with two day intervals; at each irradiation 200 roentgens was applied through a filter of 0.5 mm. of copper, with 150 kilovolts, 5 milliamperes and at a focus-skin distance of 40 cm. The next series consisted of three irradiations of 200 roentgens each; between the first and the second series there was an interval of one month. Thereafter the roentgen treatment was twice repeated with monthly pauses, a series of three separate irradiations of 200 roentgens having been given at each treatment. The authors employed this treatment in a woman aged 77 who had polycythemia. In response to this roentgen irradiation of the pylorus the erythrocytes decreased from 11 to 4.1 million and the hemoglobin dropped from 138 to 100 per cent. The color index increased from 0.6 to 1.2, the mean diameter of the red cells from 7.29 to 7.81 microns.

Ugeskrift for Læger, Copenhagen

100: 1317-1340 (Nov. 24) 1938

Determinations of Vitamin A. H. Møllgaard.—p. 1317.

Ascorbic Acid Relation of Blood Plasma and Kidney Threshold for Ascorbic Acid in Patients with Cutaneous Diseases and in Normal Persons. P. W. Bræstrup and P. Hansen.—p. 1324.

*Attempt at Preventing Serum Sickness by Aid of Ascorbic Acid. E. Schiødt and P. K. Søgaard.—p. 1327.

Attempt at Preventing Serum Sickness by Aid of Ascorbic Acid.—Schiødt and Søgaard's material comprises sixteen pneumonia patients given serum treatment. While the seven control patients all had serum sickness, three of the nine patients in whom daily doses intravenously of from 100 to 200 mg. of ascorbic acid were administered for from five to eighteen days after the temperature had fallen had no serum sickness and six developed it in only slight degree.